

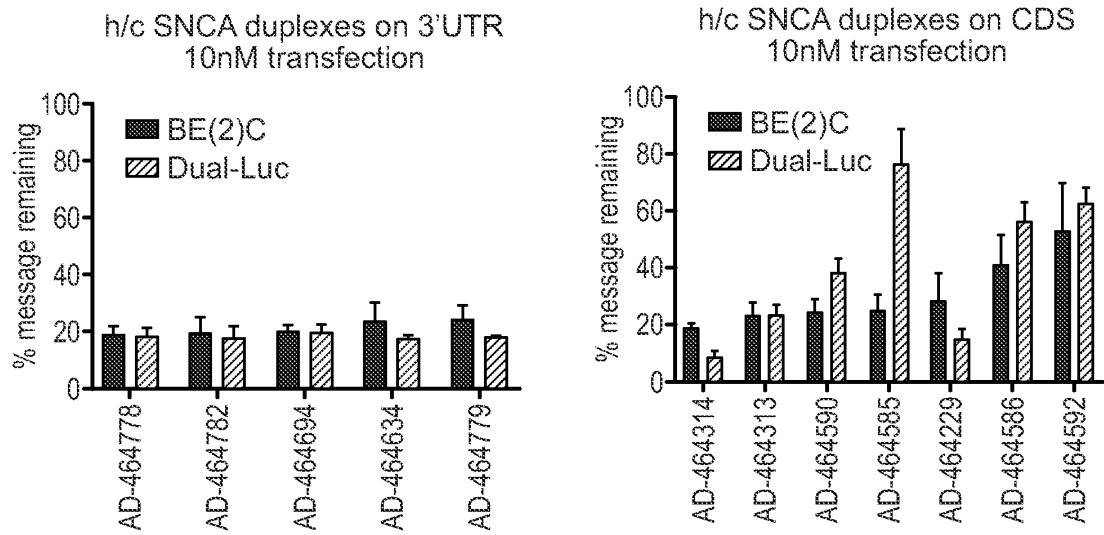


FIG. 1A

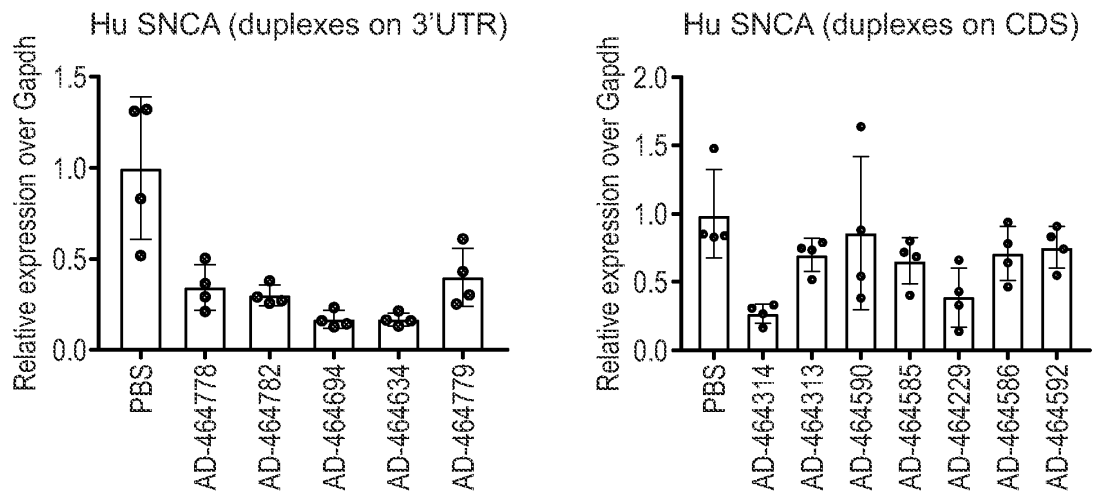


FIG. 1B

Top 40 most potent SNCA targeting duplexes from Hot Spot + SAR set

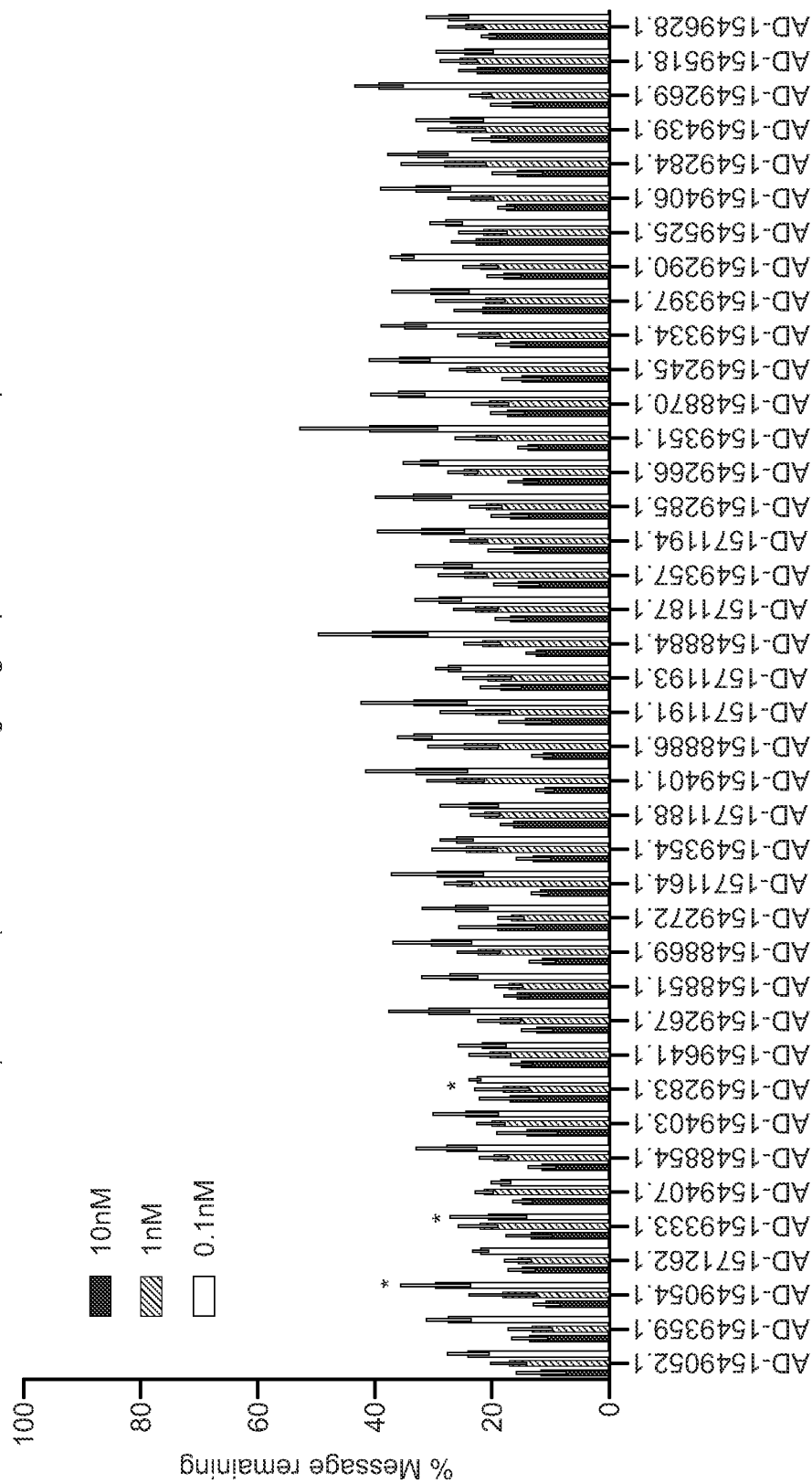
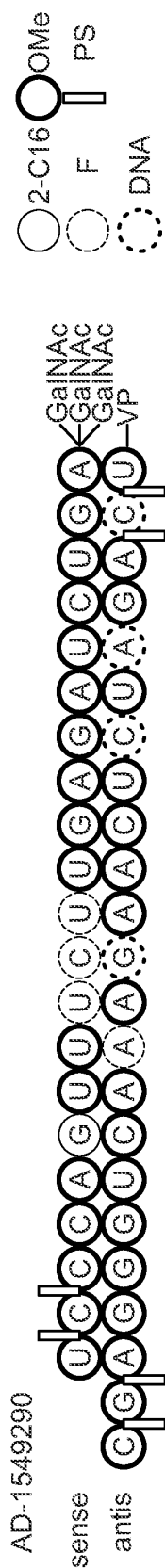
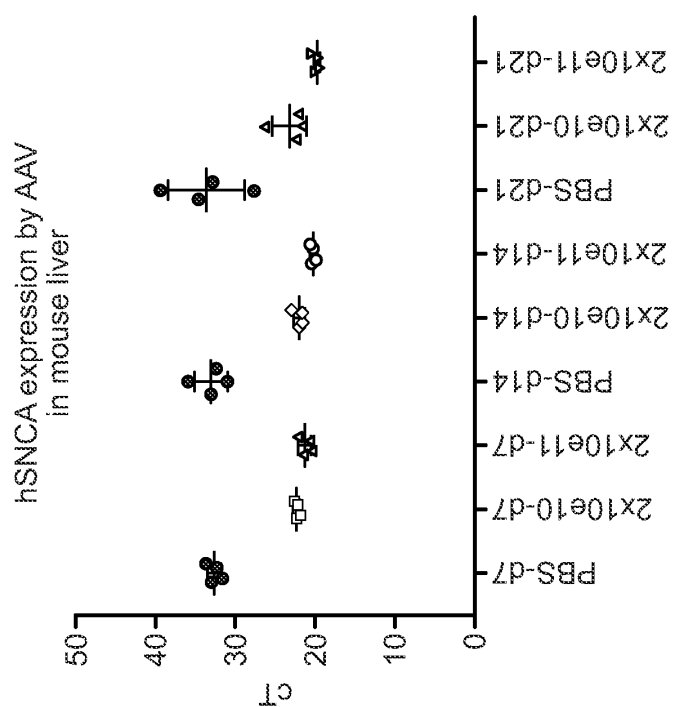
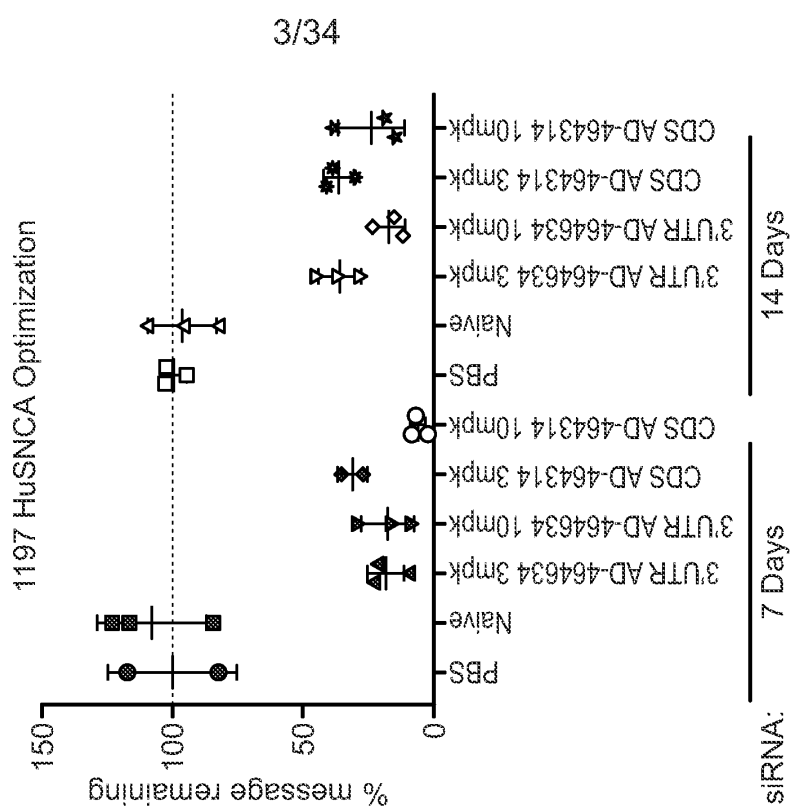


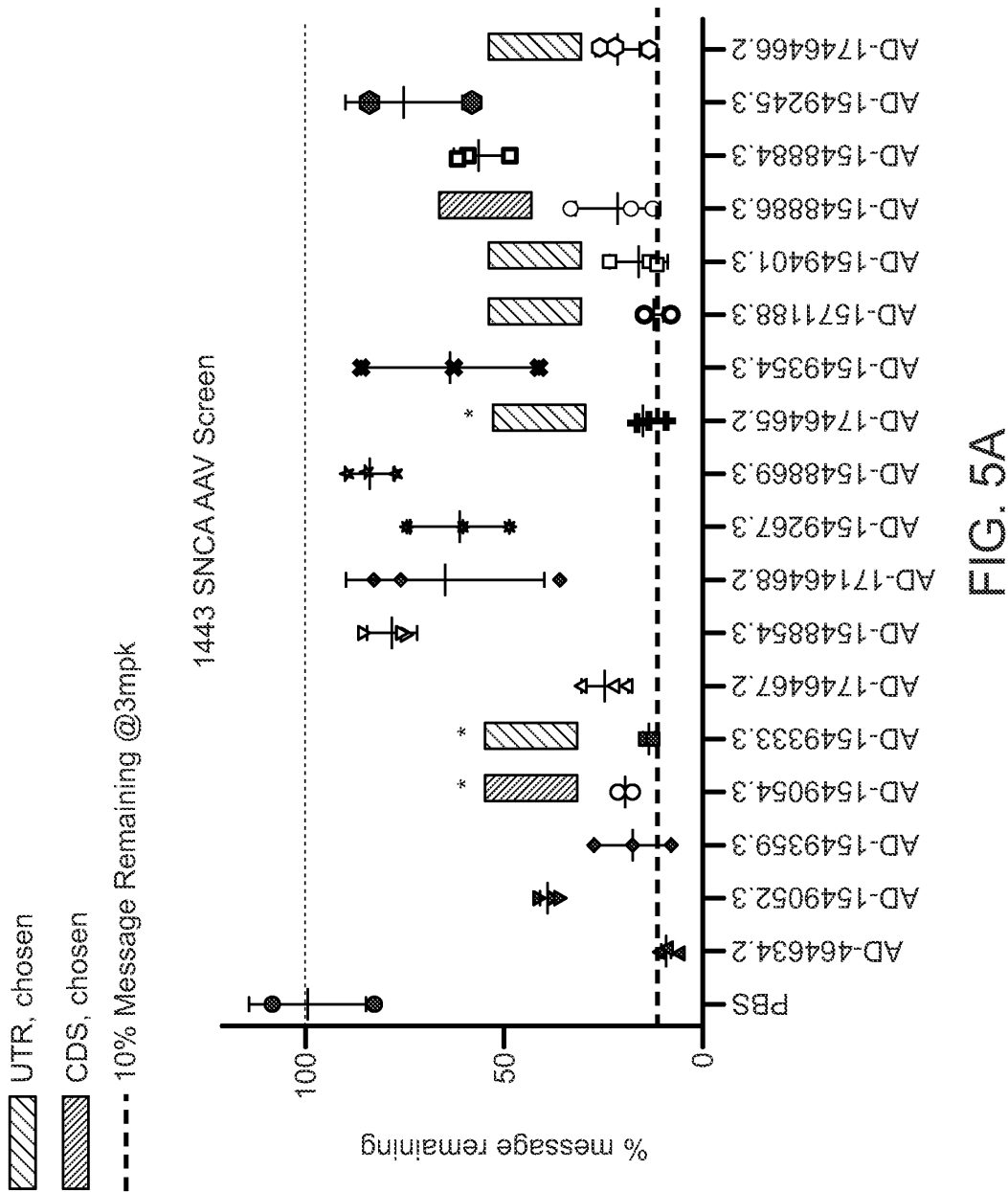
FIG. 2

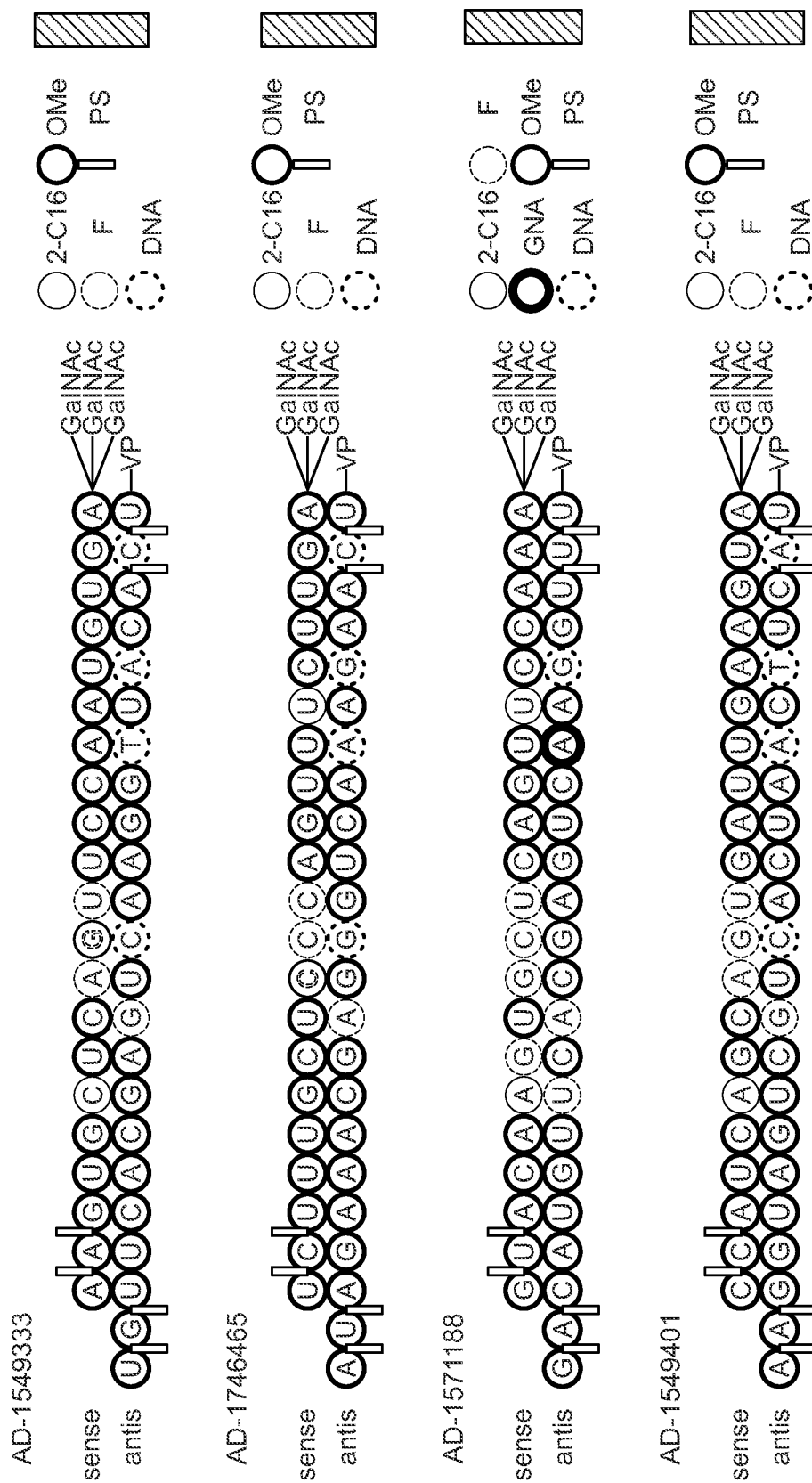




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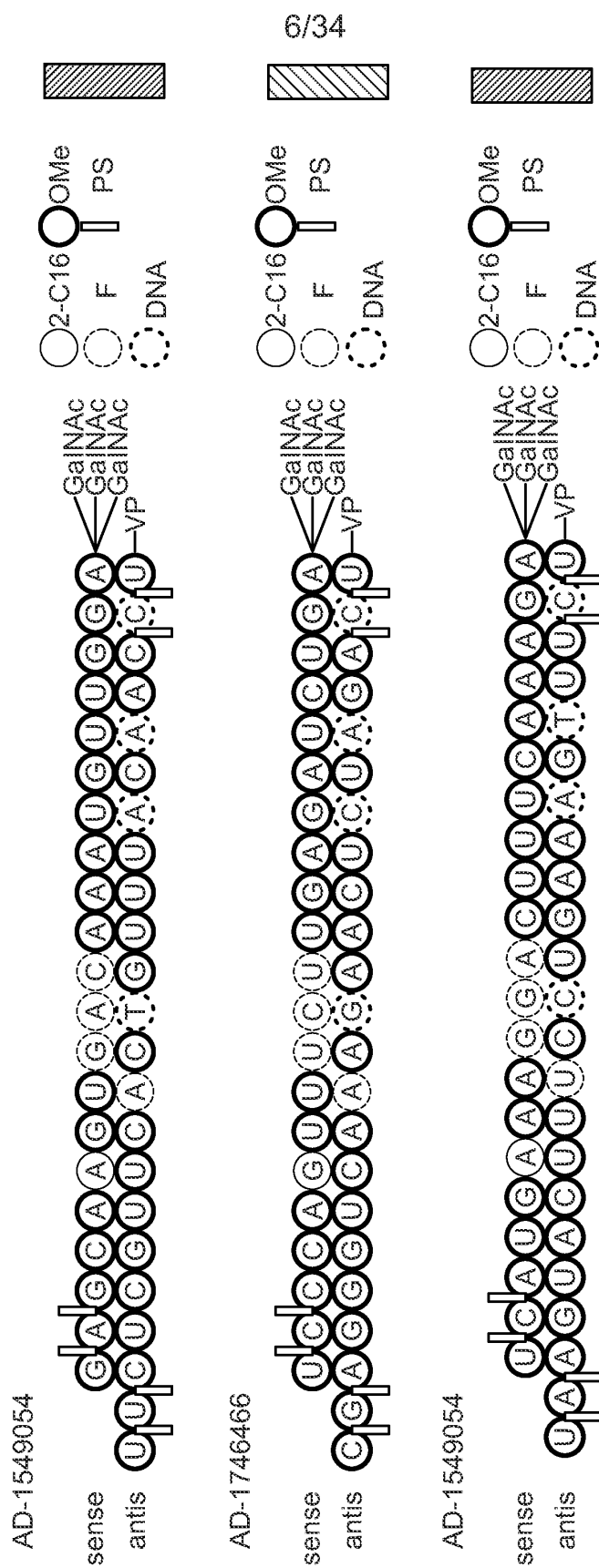


FIG. 5B (cont)

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Identifier	Location	In vivo (% Message Remaining @3mpk)	ED ₈₀ (nM)
AD-1549333	UTR	9.06	0.235
AD-1746465	UTR	13.43	0.405
AD-1571188	UTR	12.37	1.075
AD-1549401	UTR	16.03	1.216
AD-1549054	CDS	18.62	0.504
AD-1746466	UTR	21.41	2.871
AD-1548886	CDS	21.49	1.210

FIG. 6A

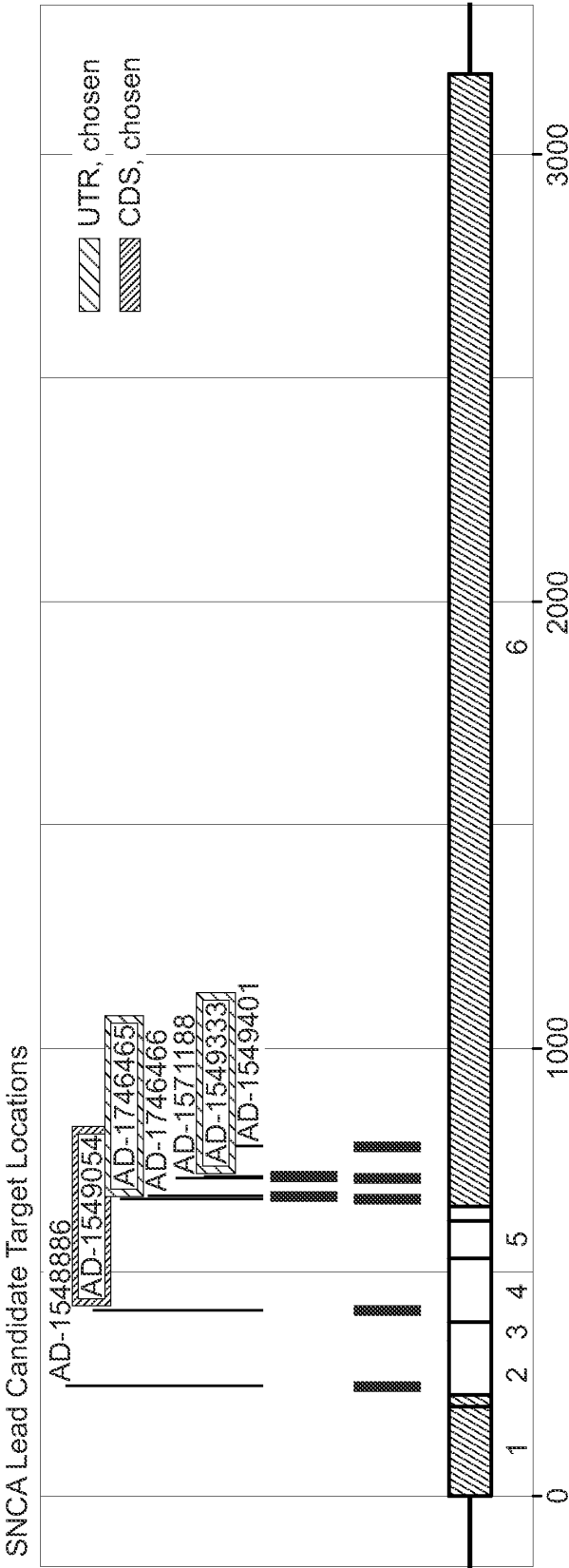
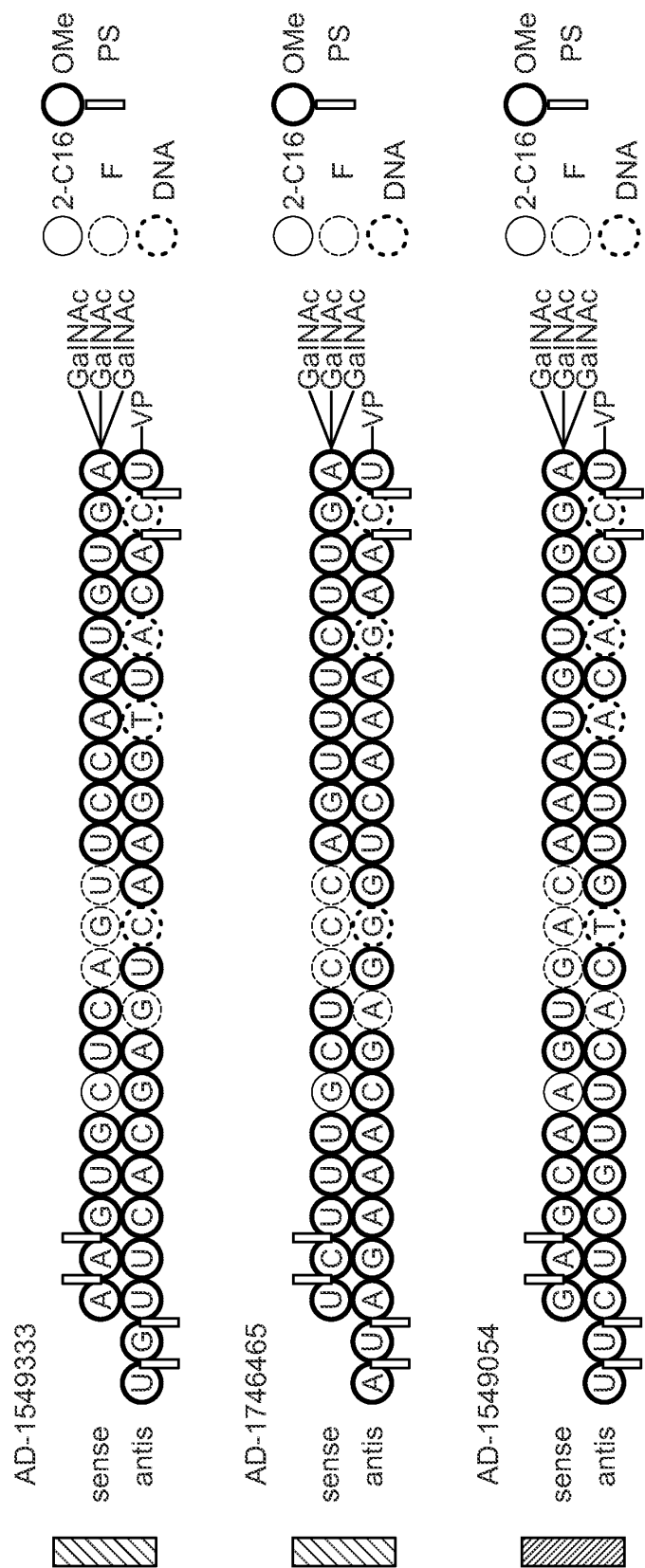


FIG. 6B



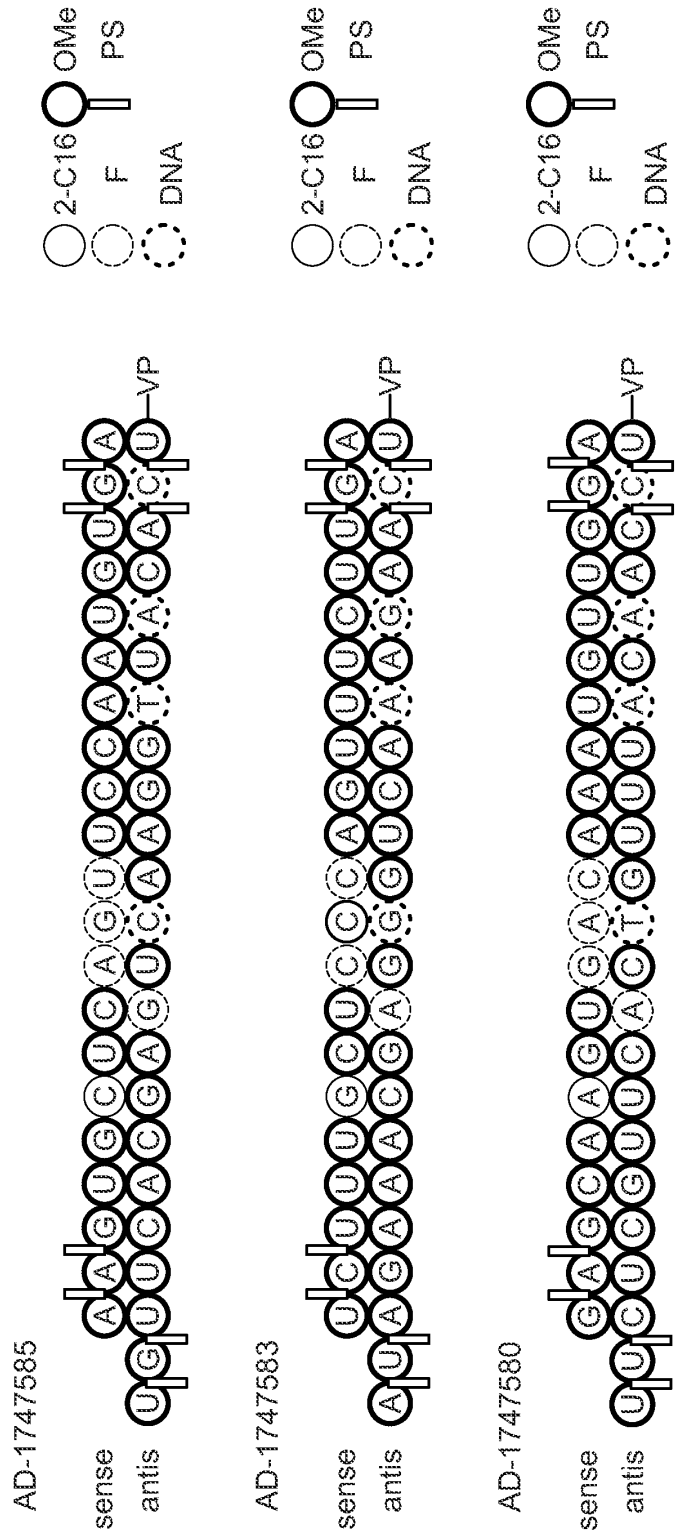


FIG. 7

Identifier	Location	In vivo (% Message Remaining @3mpk)	ED ₈₀ (nM)
AD-1747585	UTR	9.06	0.235
AD-1747583	UTR	13.43	0.405
AD-1747580	CDS	18.62	0.504

FIG. 8A

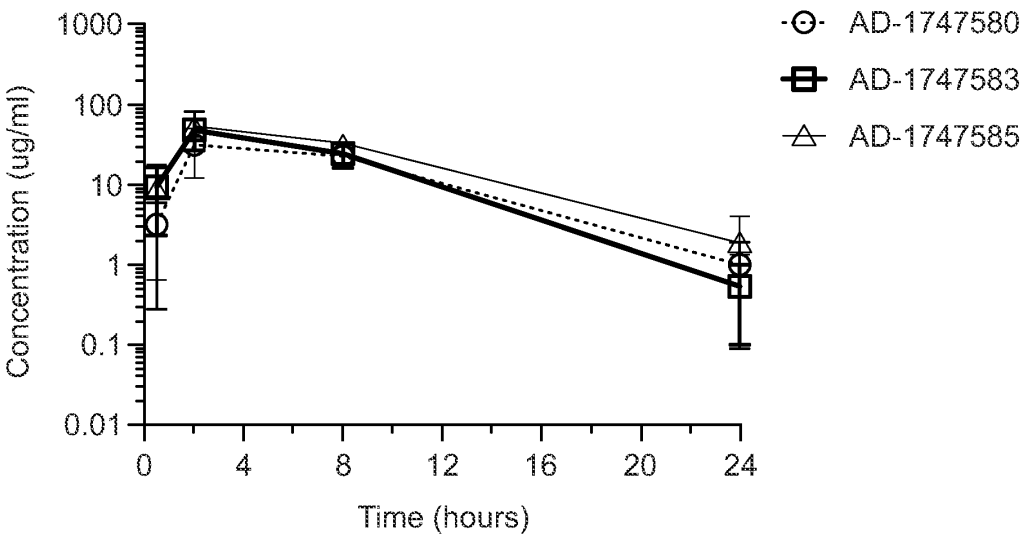


FIG. 8B

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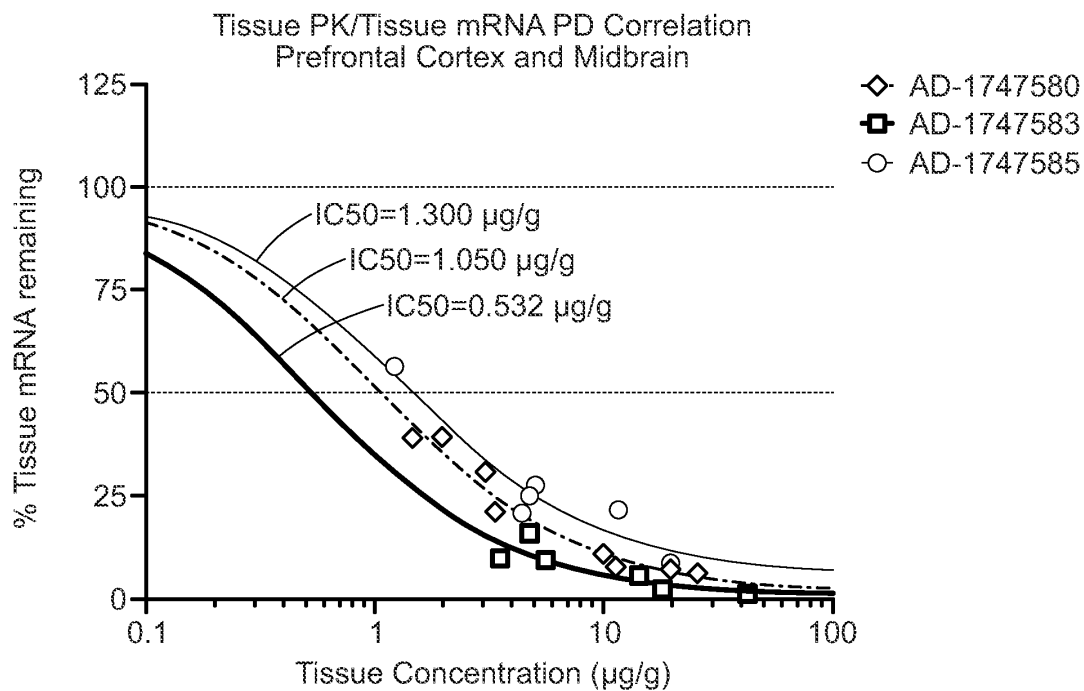
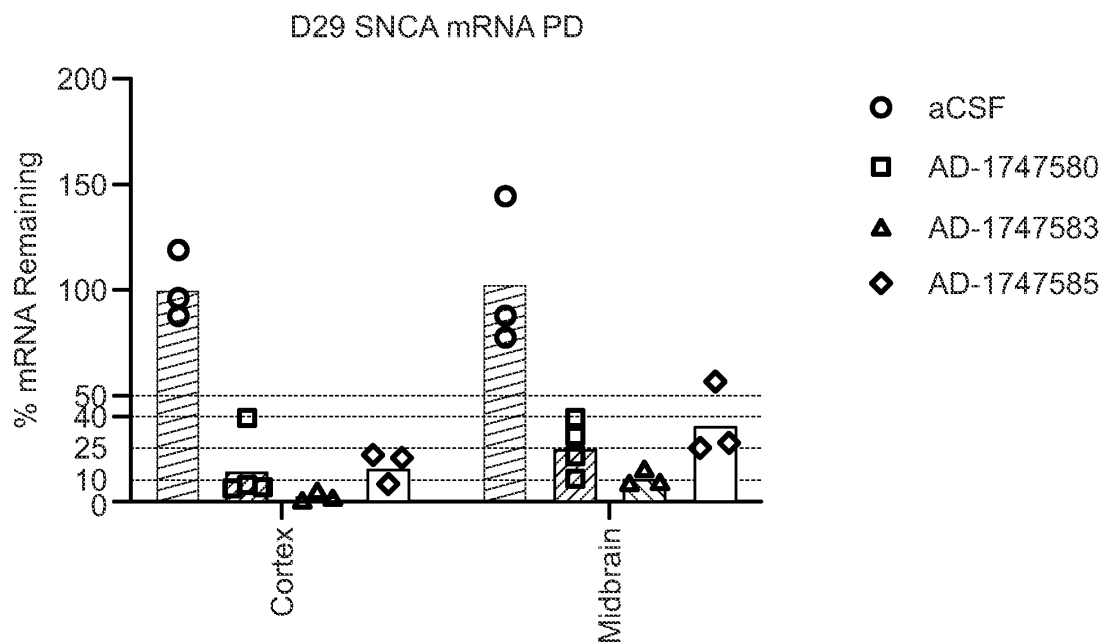


FIG. 9A

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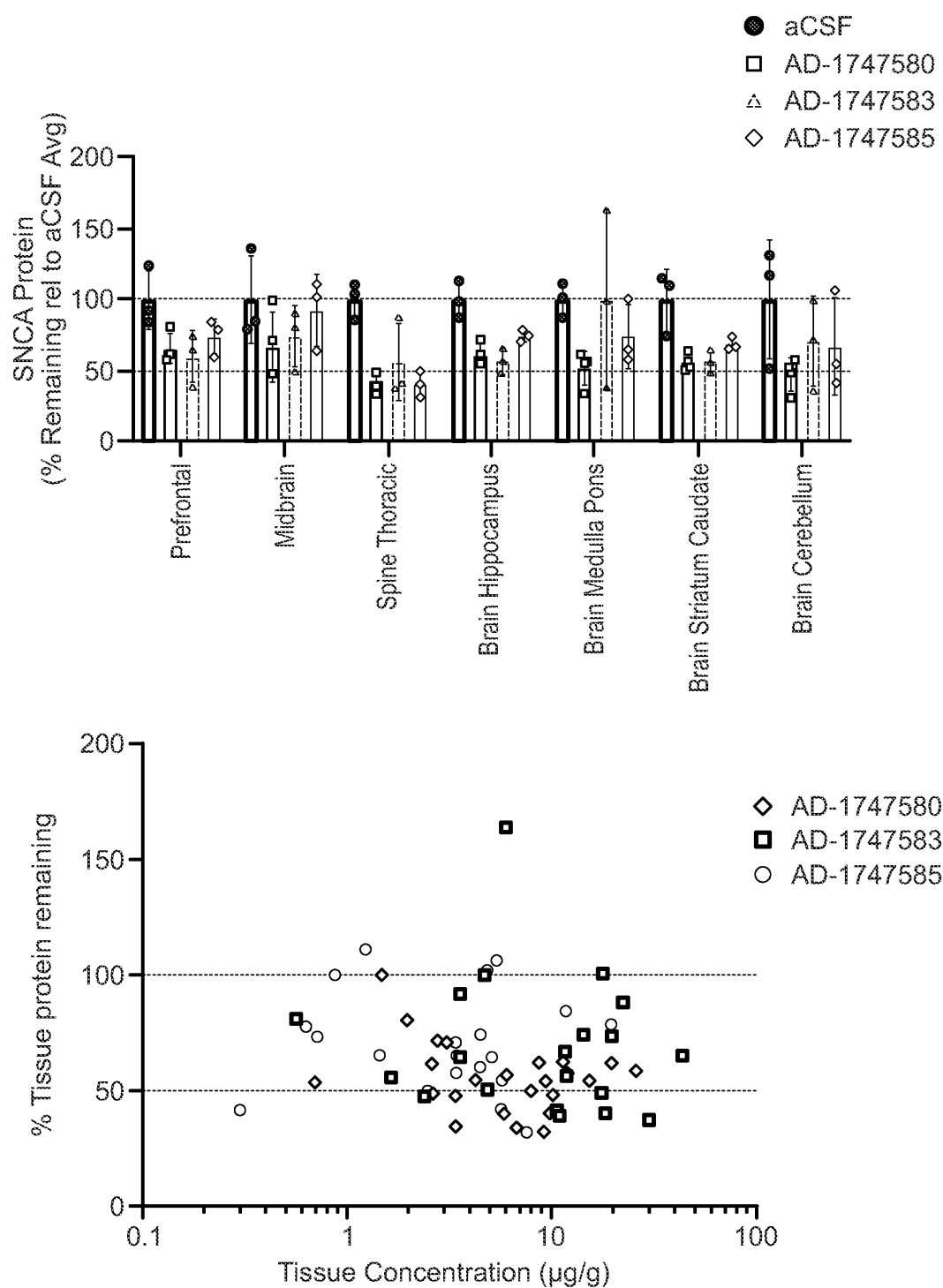
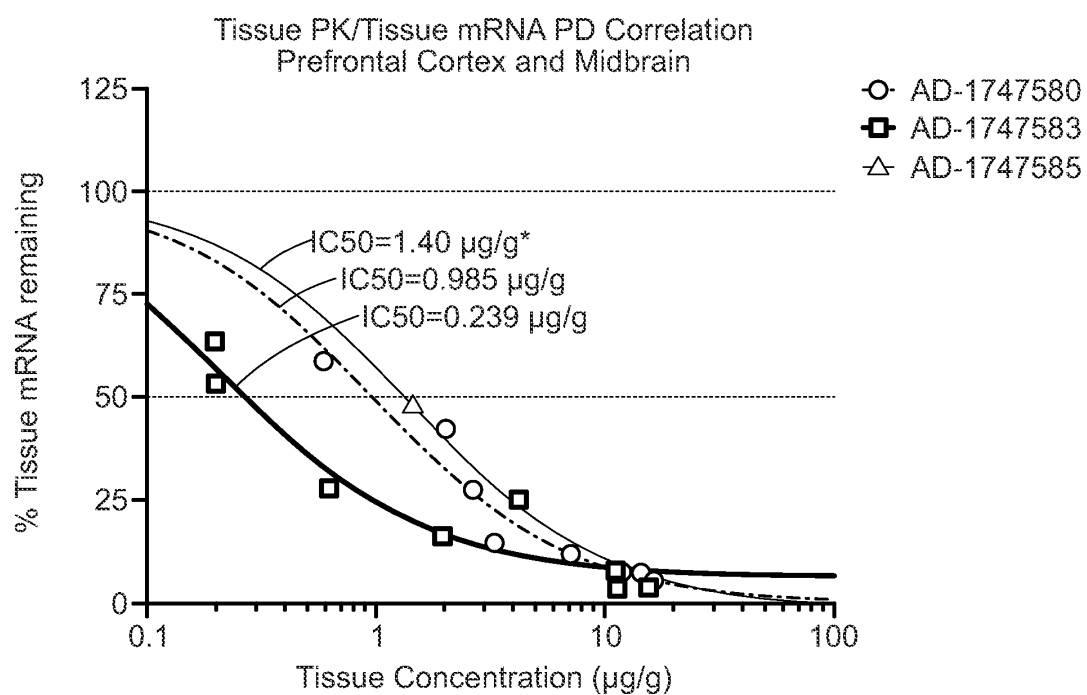
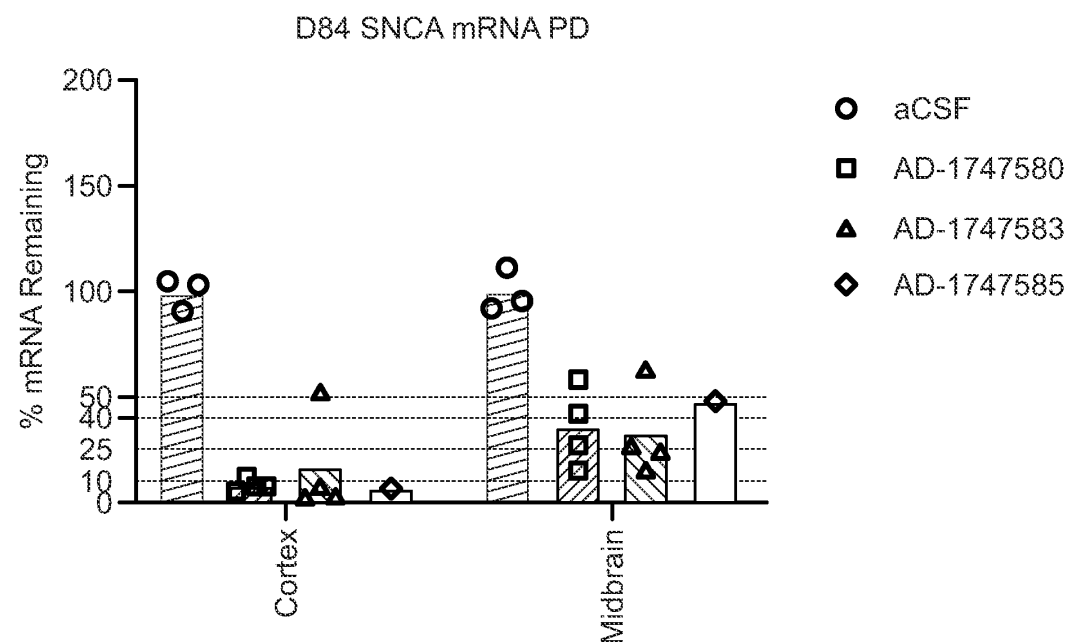


FIG. 9B

Identifier	Location	Average %NHP mRNA knockdown Cortex	Average %NHP mRNA knockdown Midbrain	Average %NHP protein knockdown D29	Average %NHP tissue protein knockdown Cortex	Average %NHP tissue protein knockdown Midbrain
AD-1747585	UTR	83.1	63.80	N/A	25.73	7.67
AD-1747583	UTR	97.09	88.42	64.72	40.17	25.73
AD-1747580	CDS	84.98	74.57	67.08	34.25	33.3

FIG. 10

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* 2 data points

FIG. 11

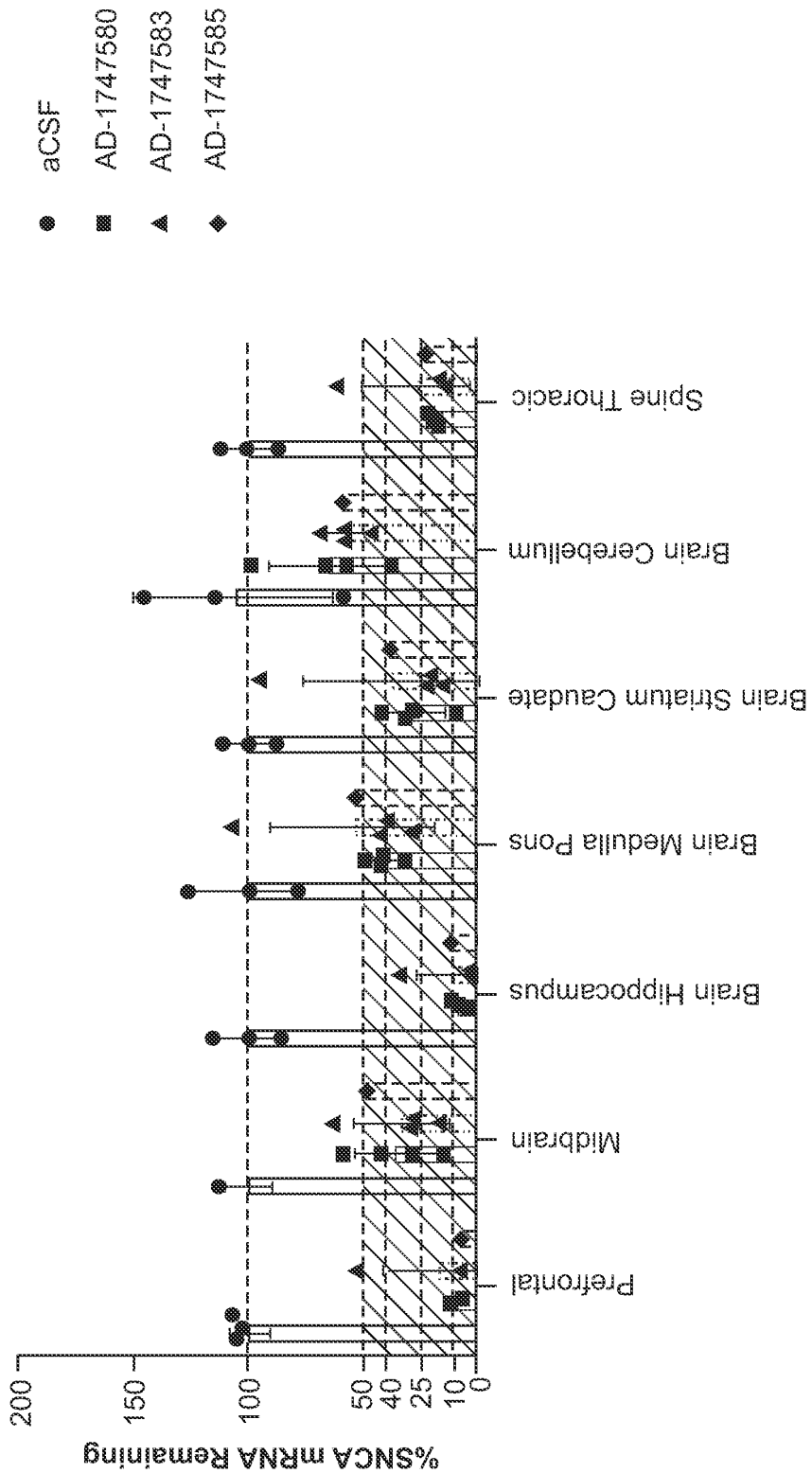


FIG. 12A

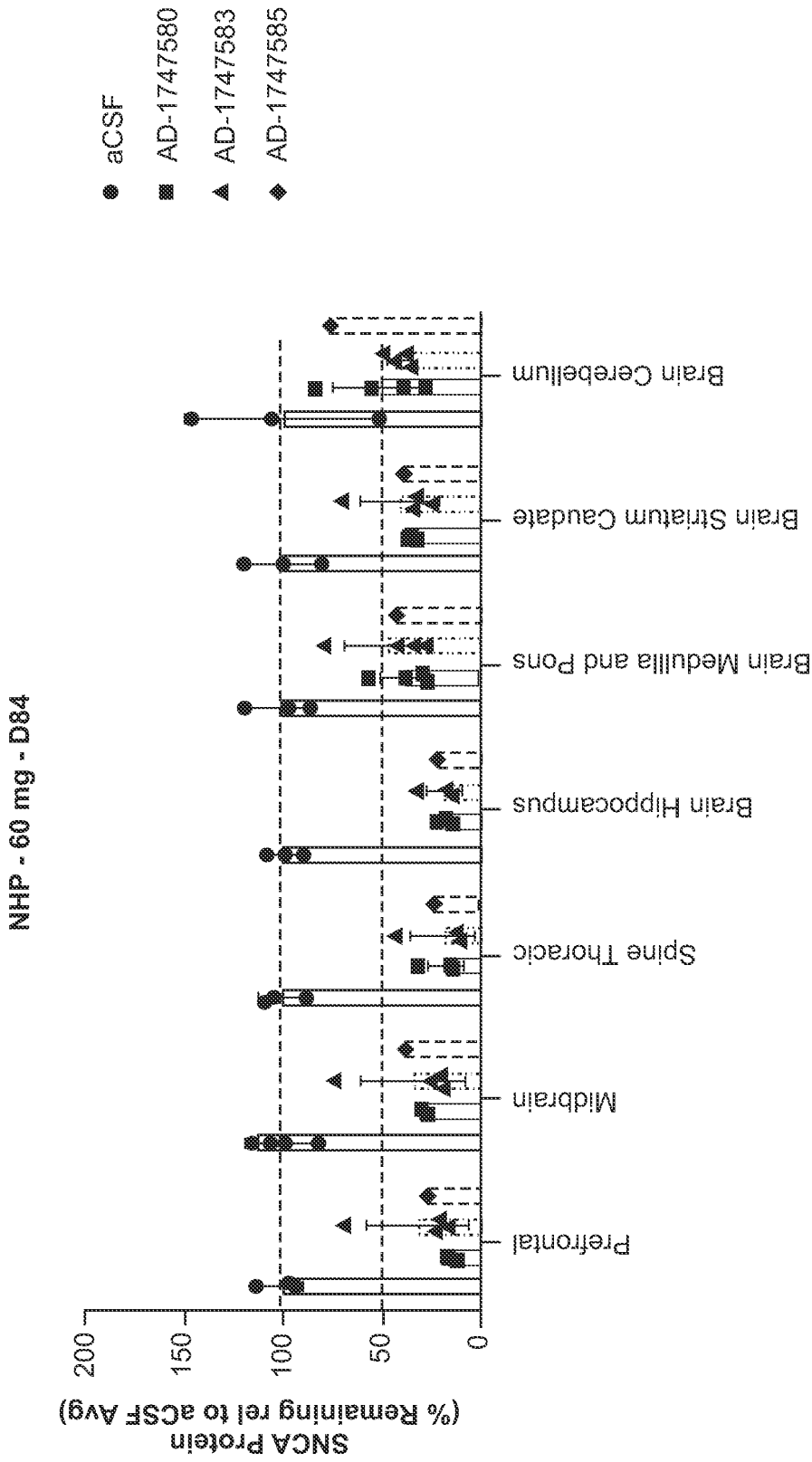


FIG. 12B

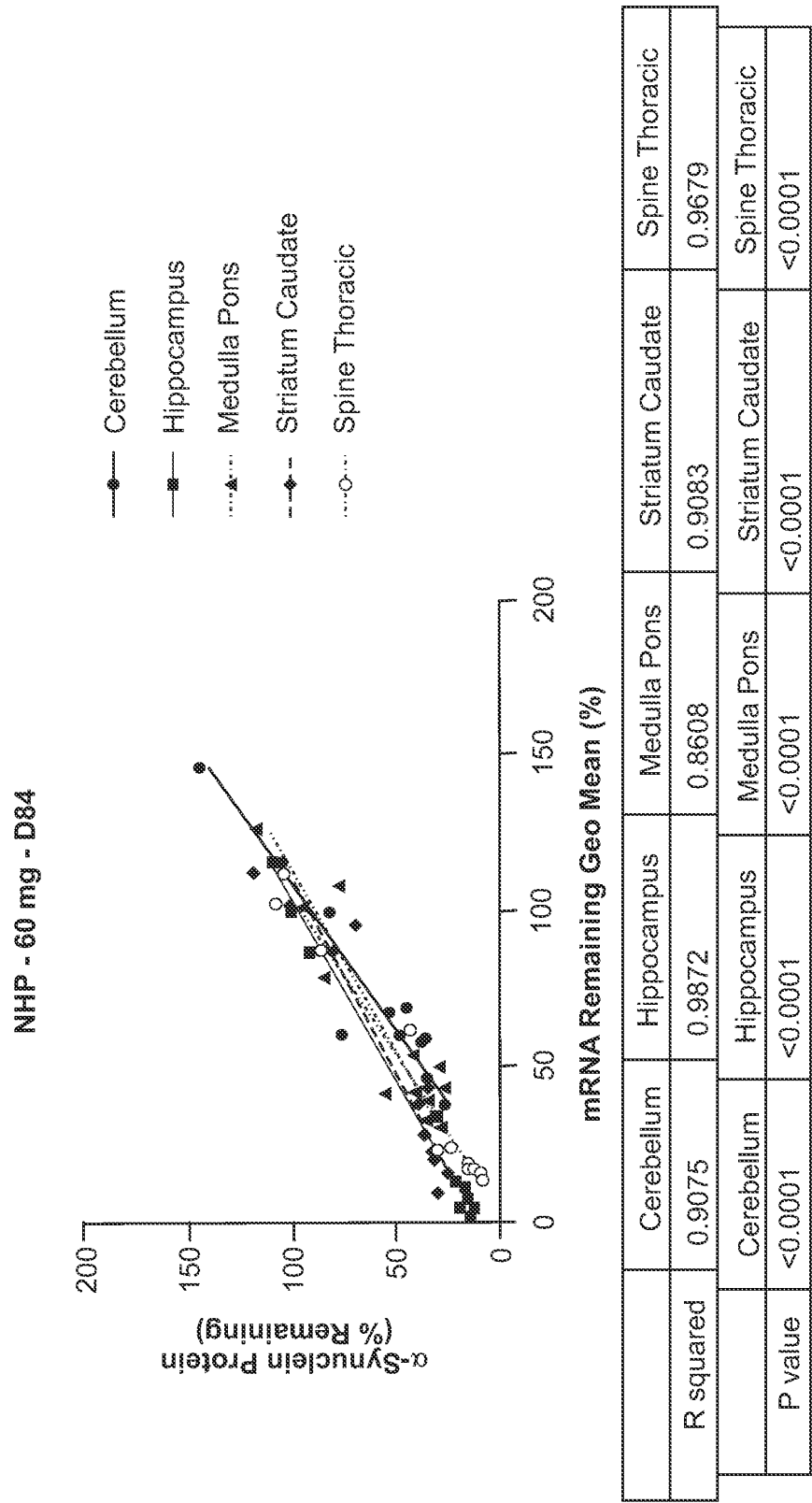


FIG. 12C

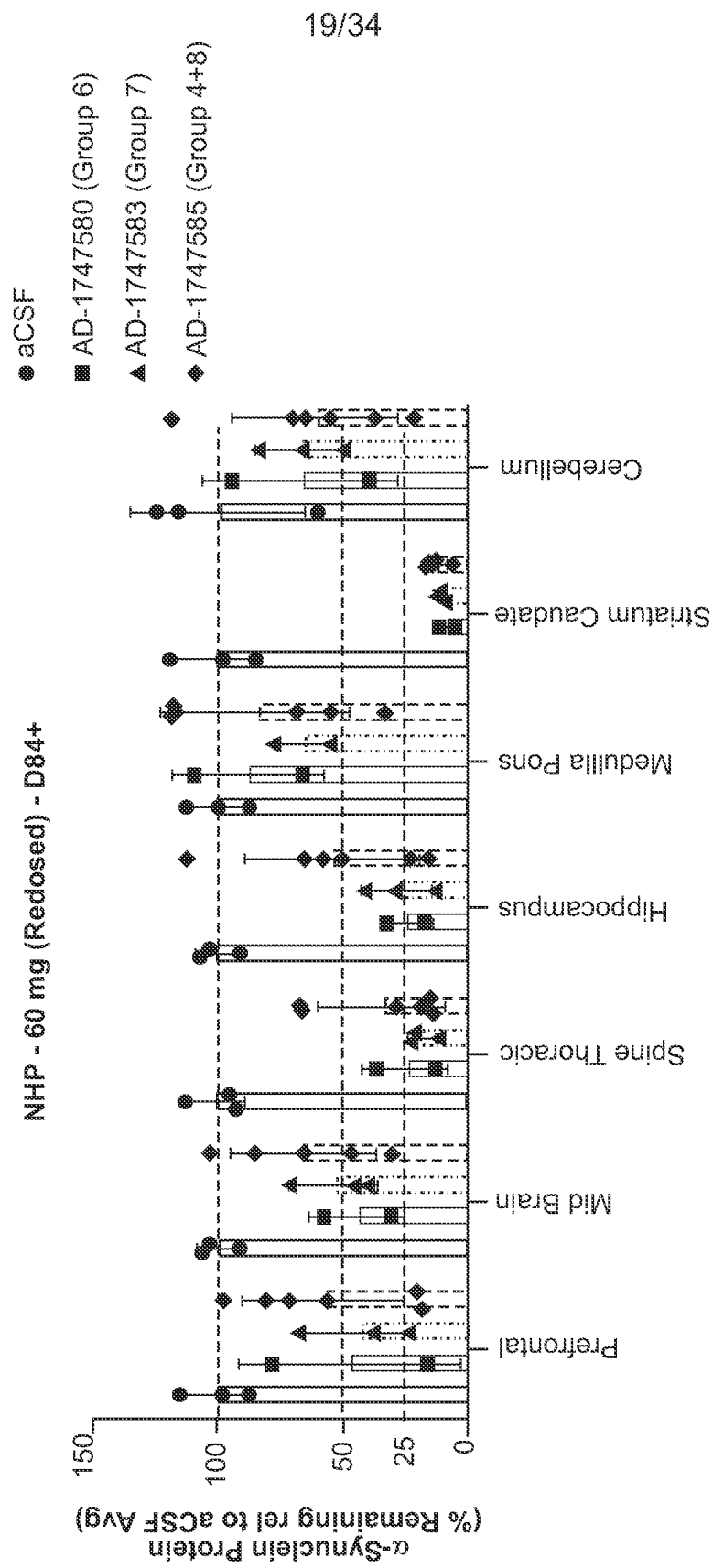


FIG. 12D

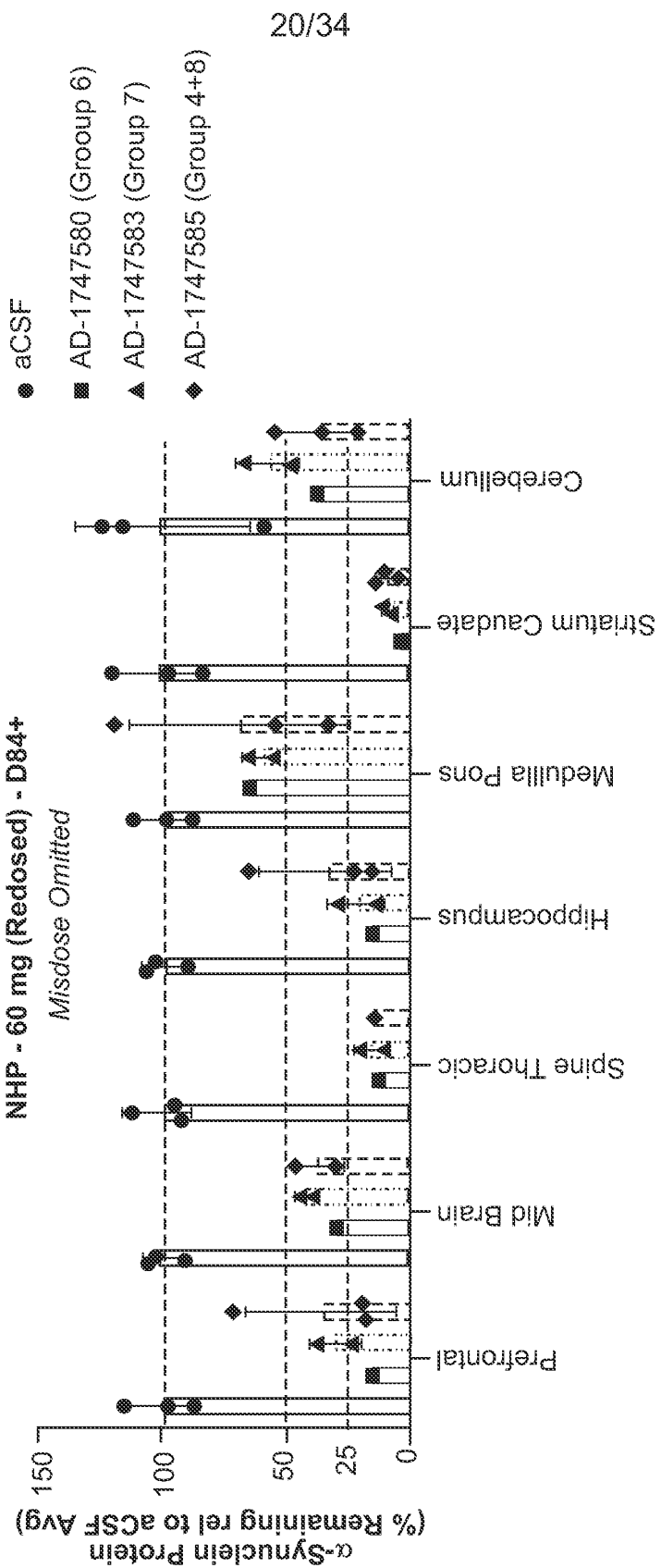
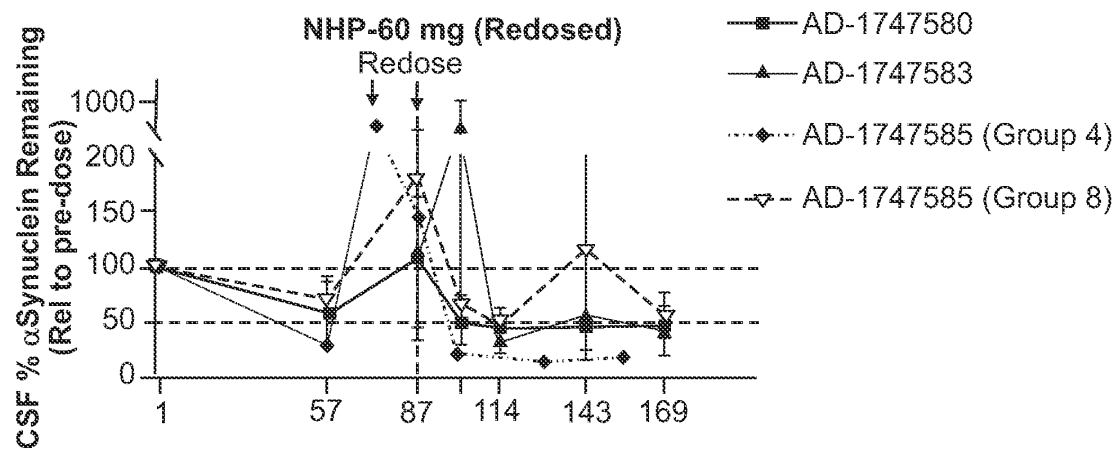
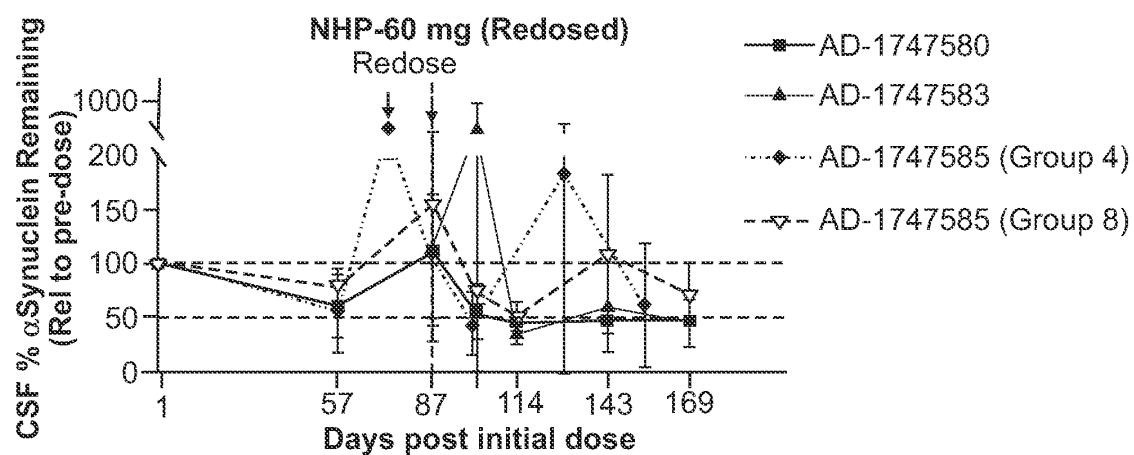


FIG. 12D (CONT)

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Animals with misdose omitted based on 24H CSF [ng/mL]

FIG. 12E

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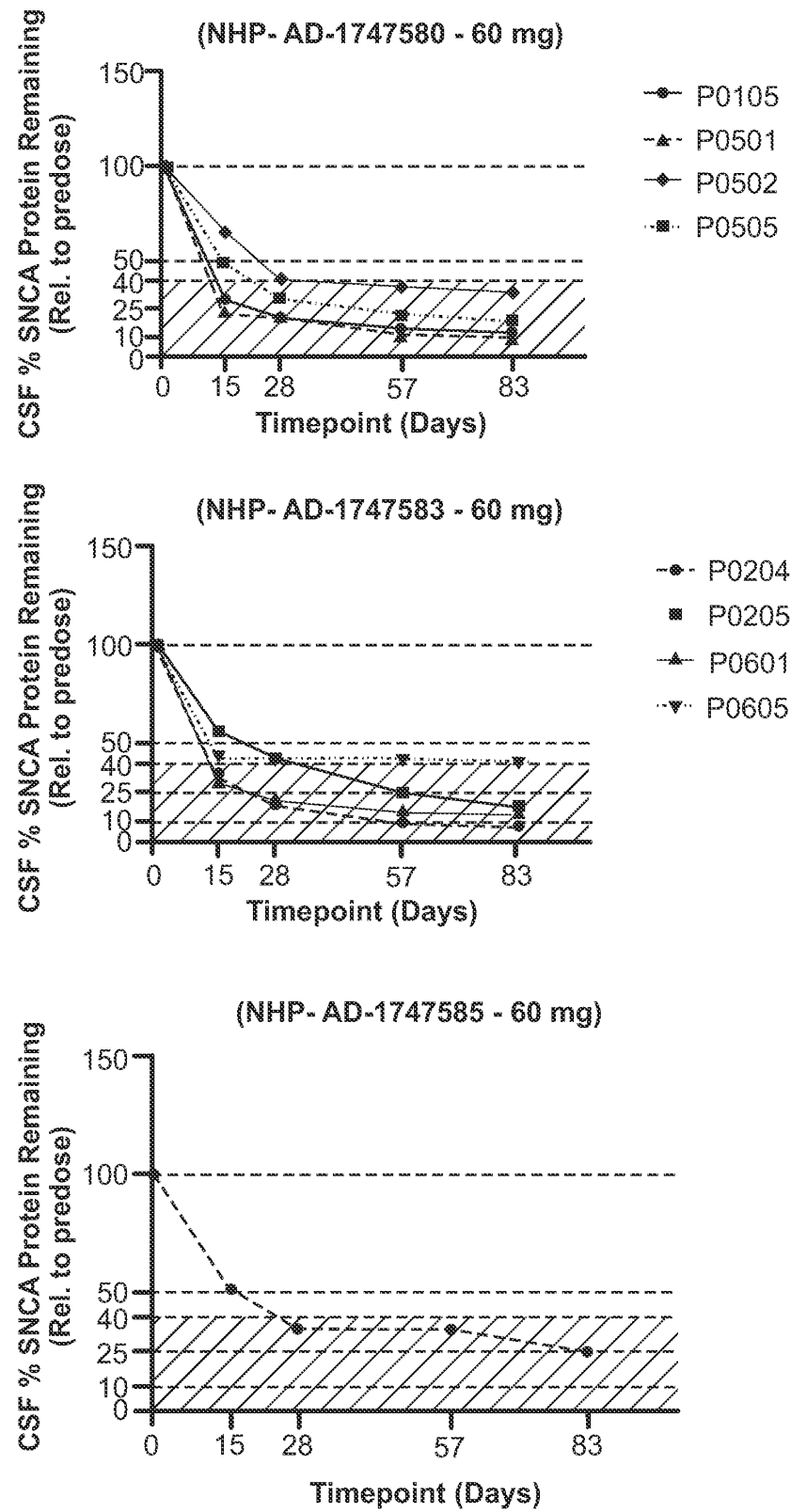


FIG. 13

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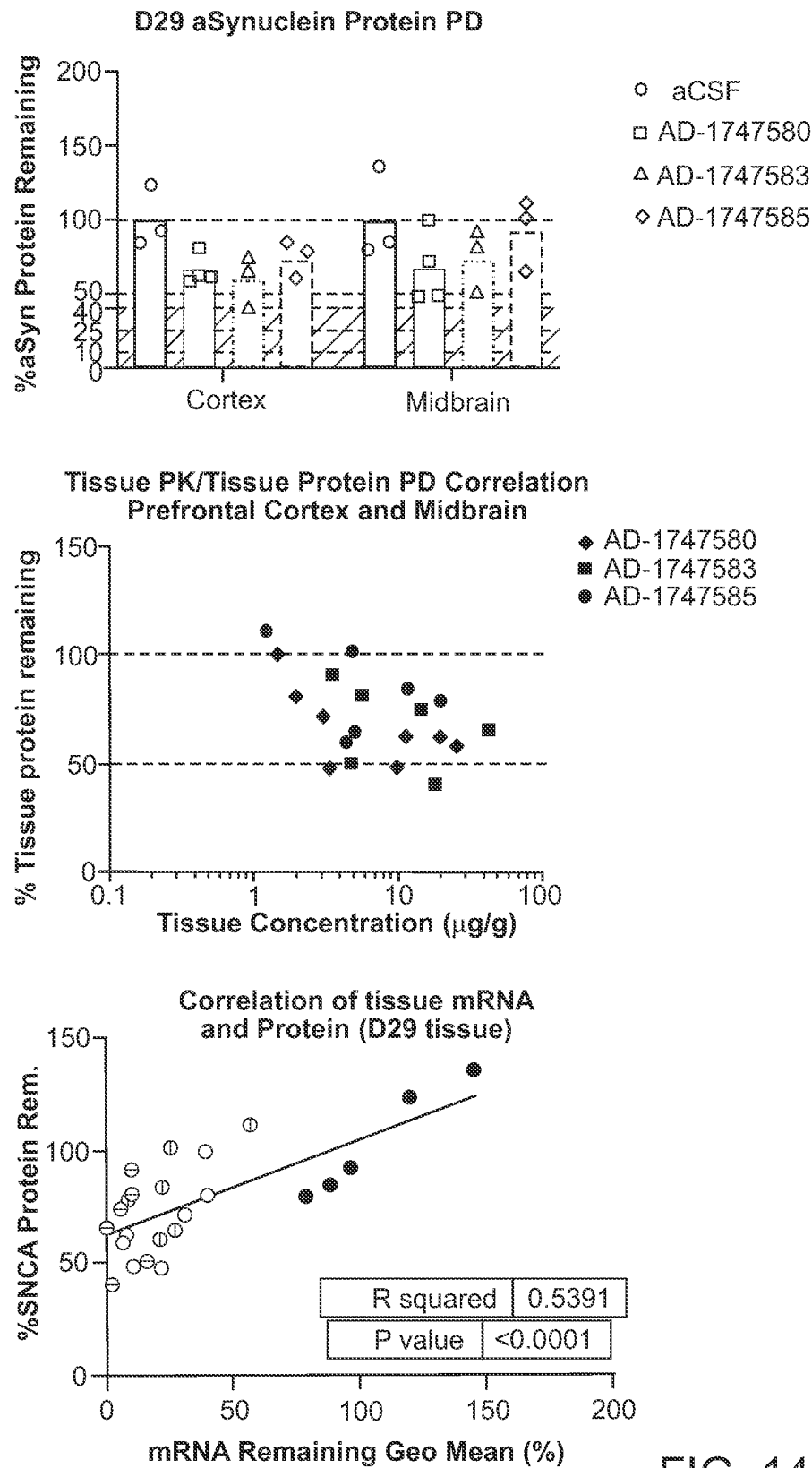


FIG. 14A

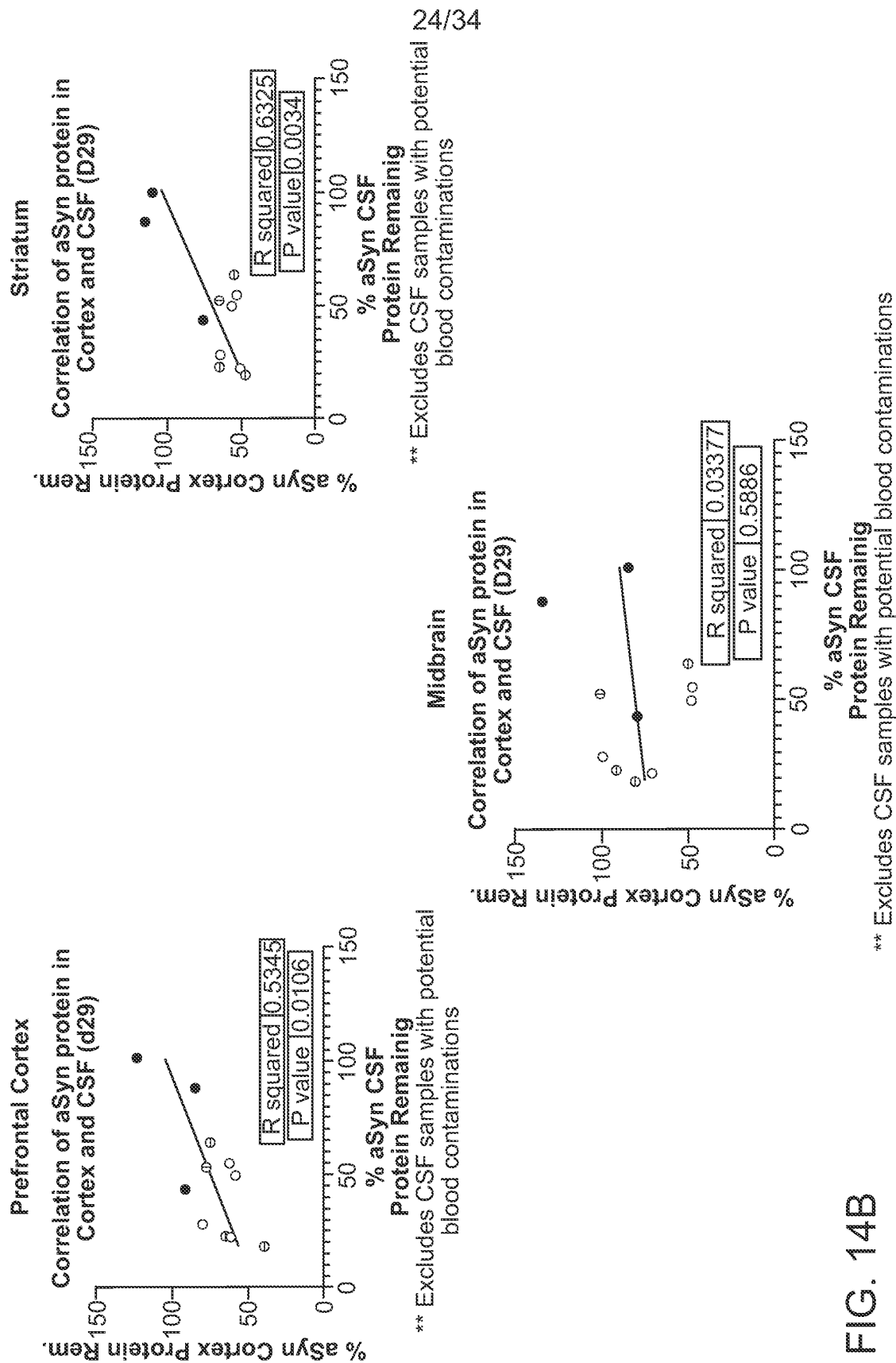


FIG. 14B

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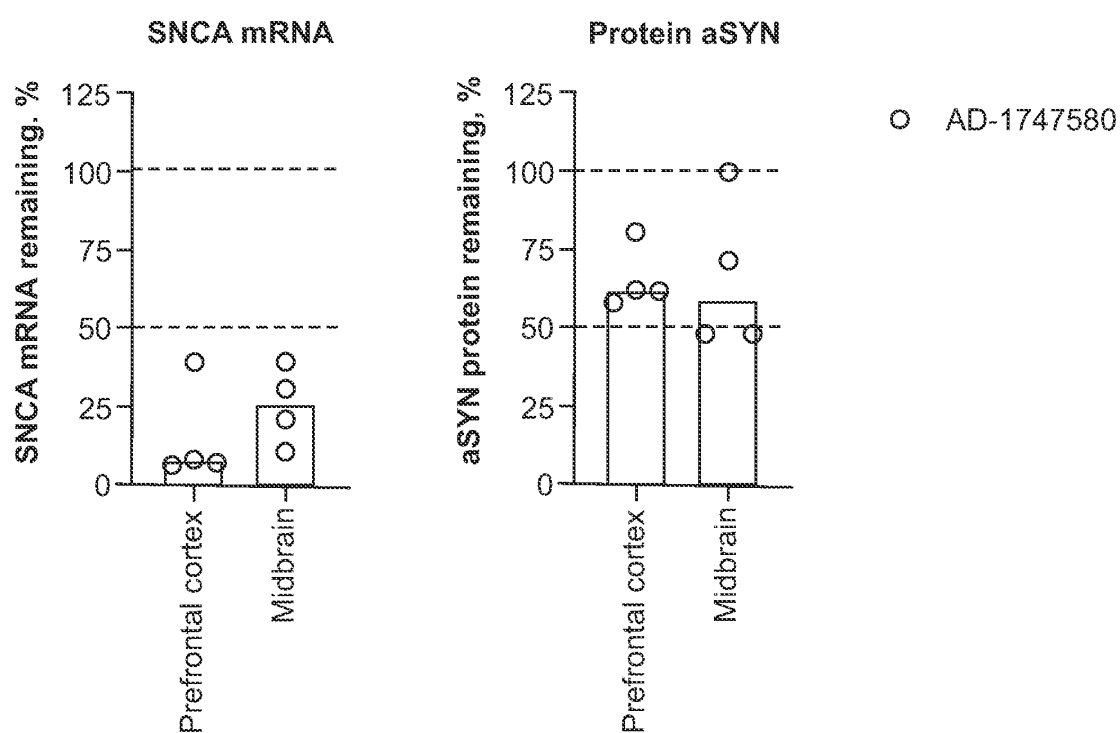


FIG. 14C

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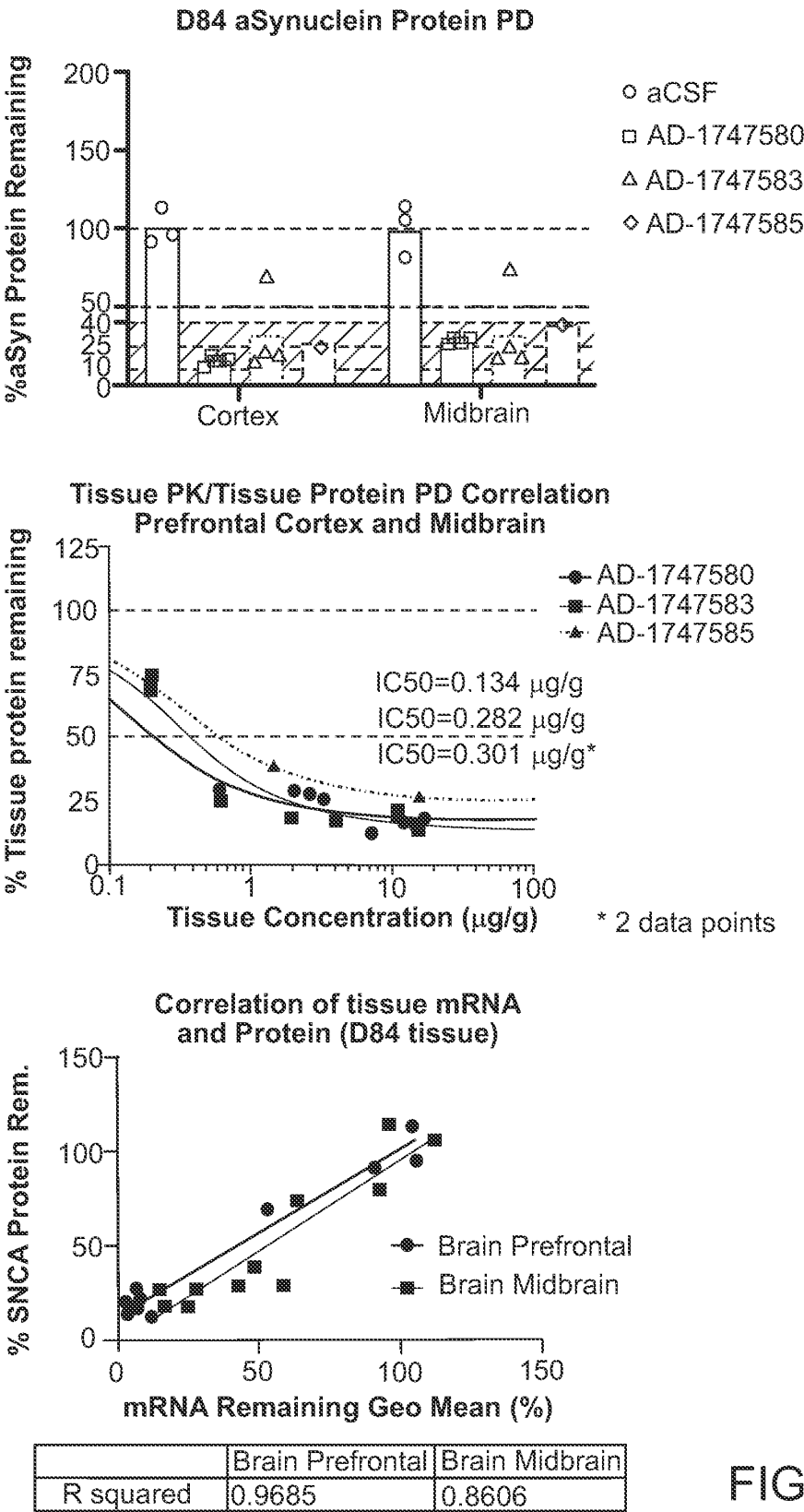


FIG. 14D

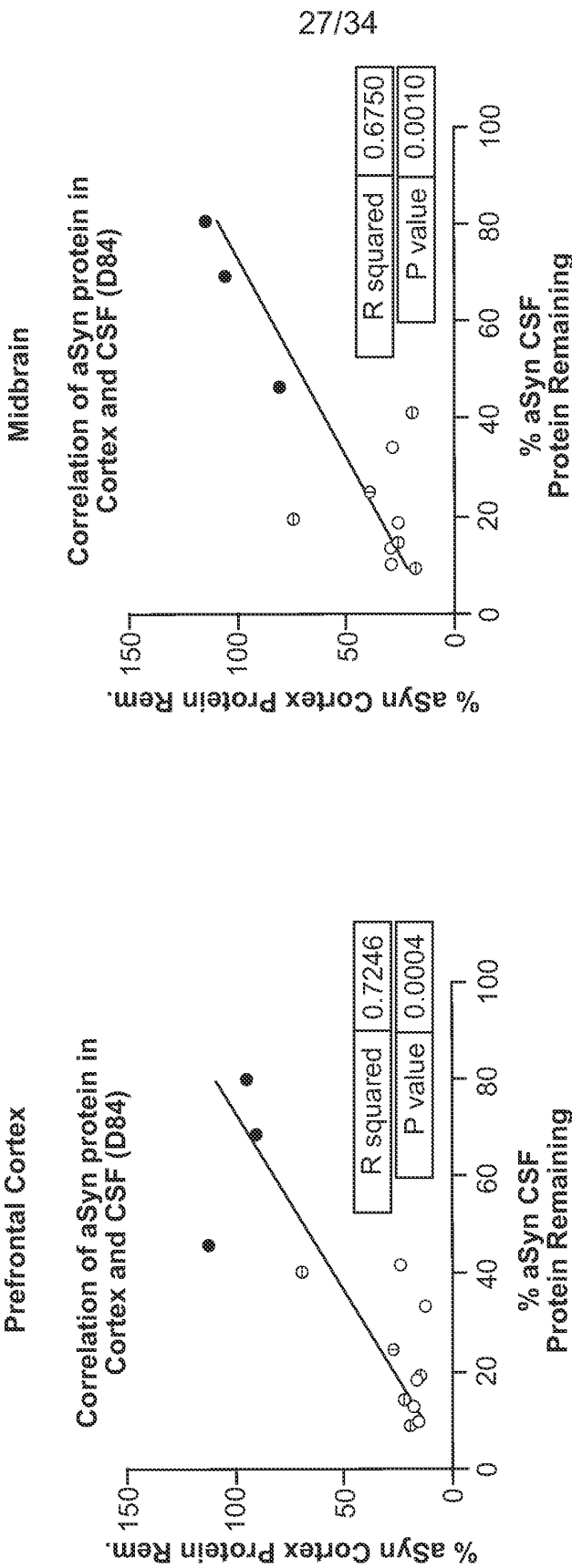


FIG. 15

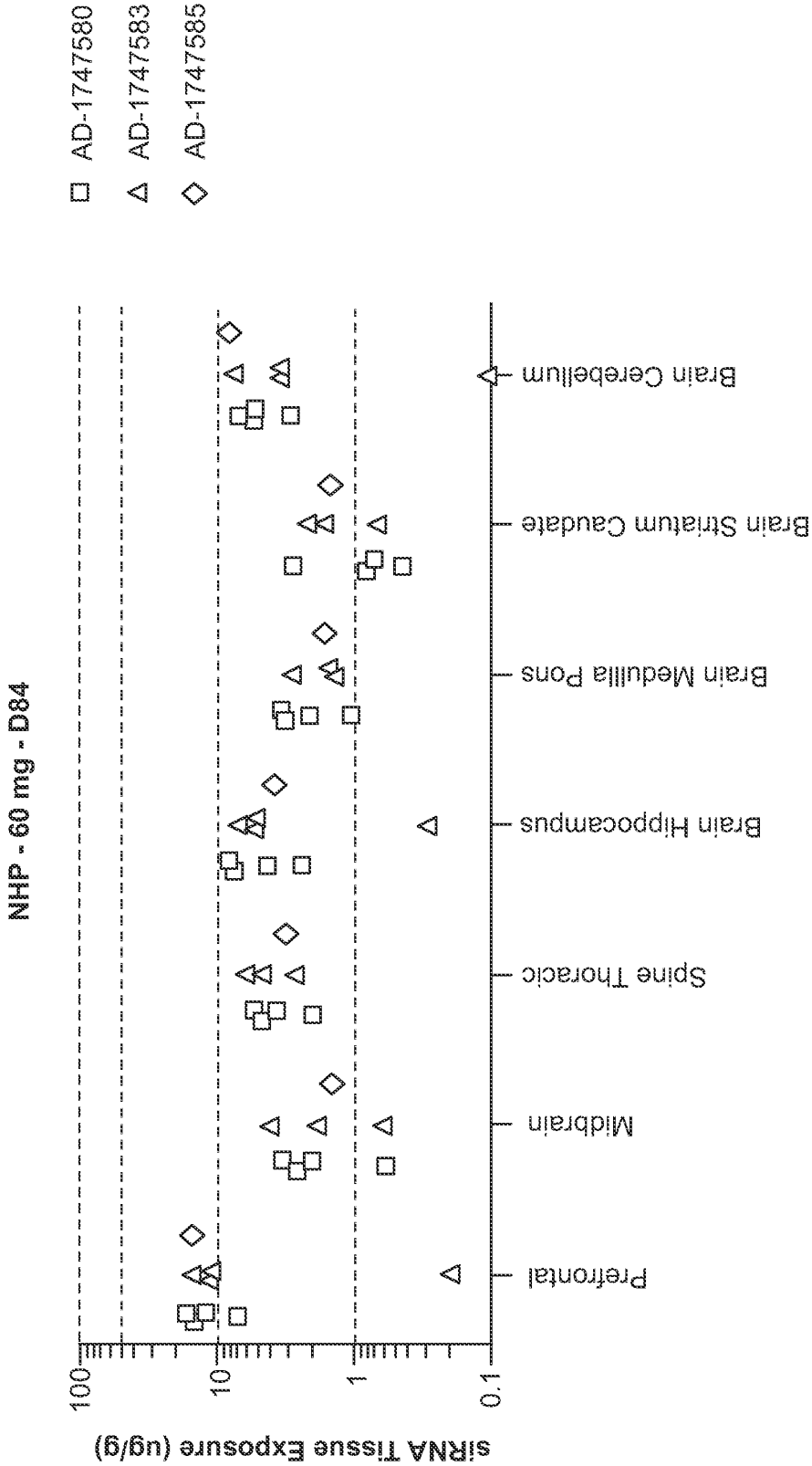


FIG. 16

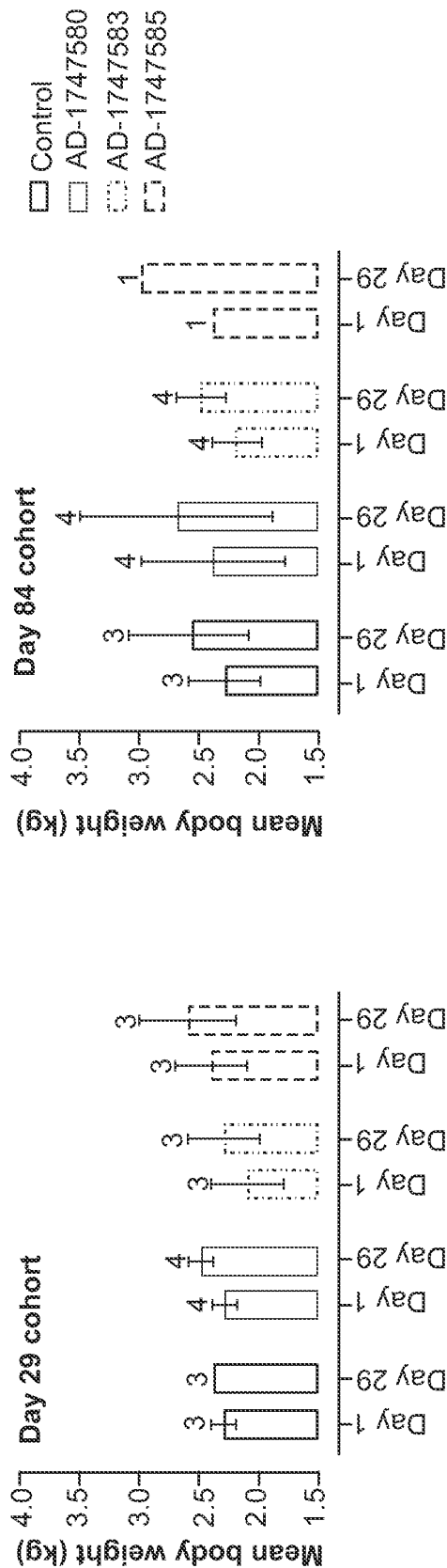


FIG. 17

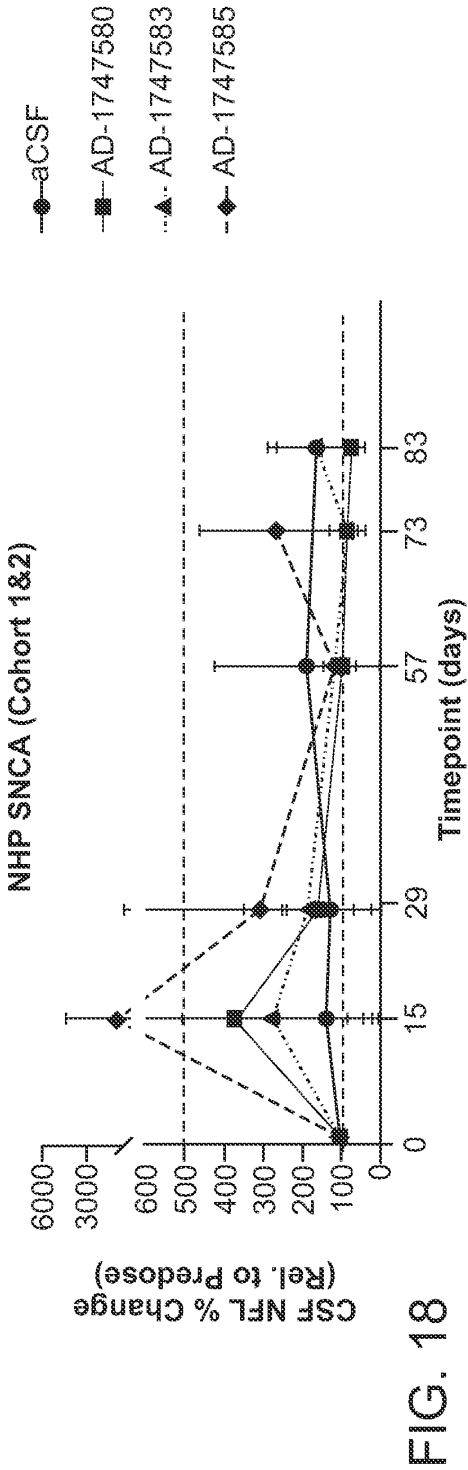


FIG. 18

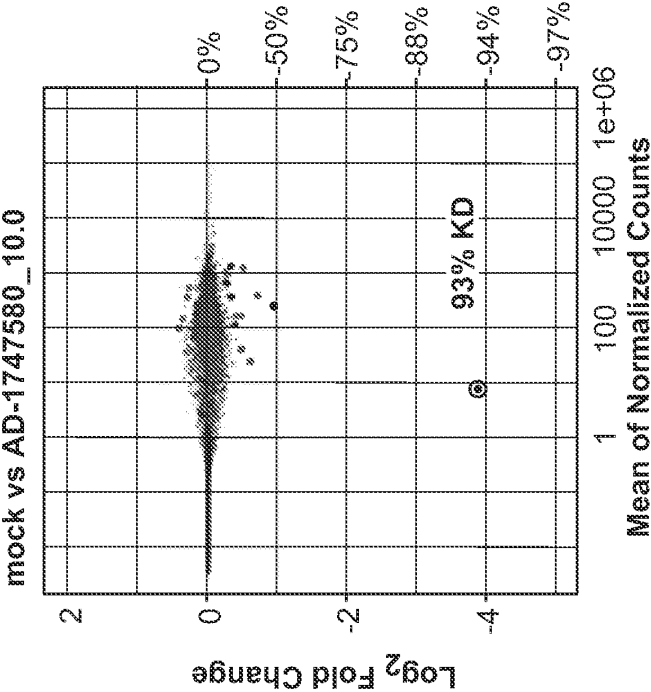
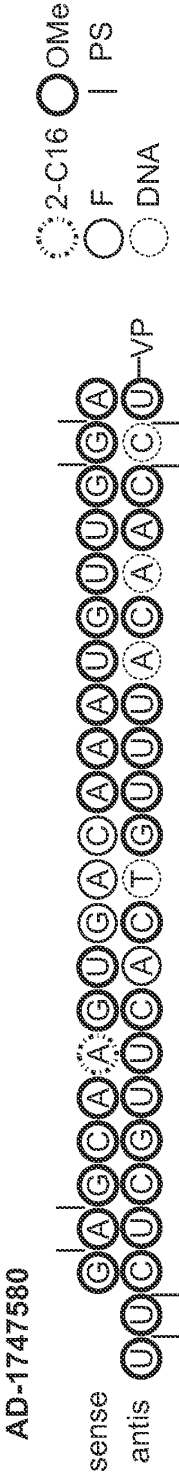
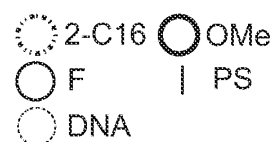
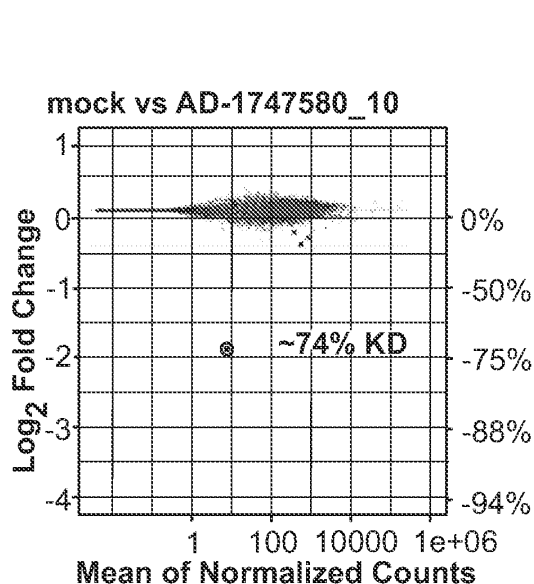


FIG. 19A

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AD-1549054



AD-1747580

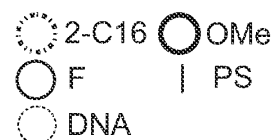
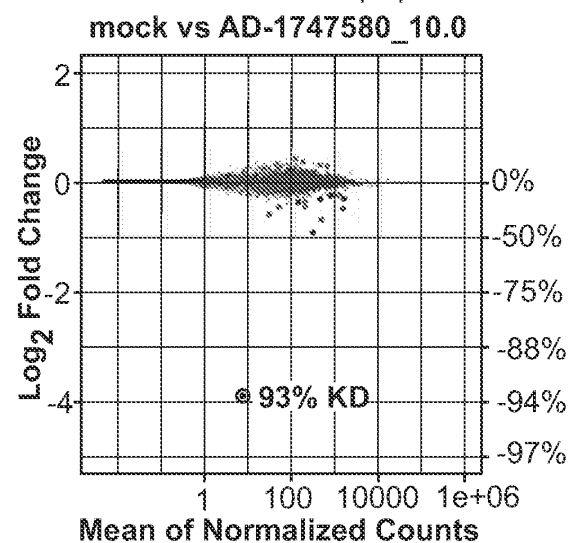
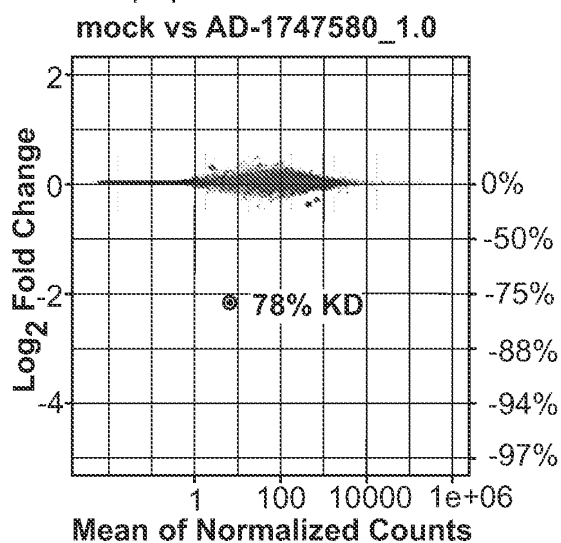


FIG. 19B

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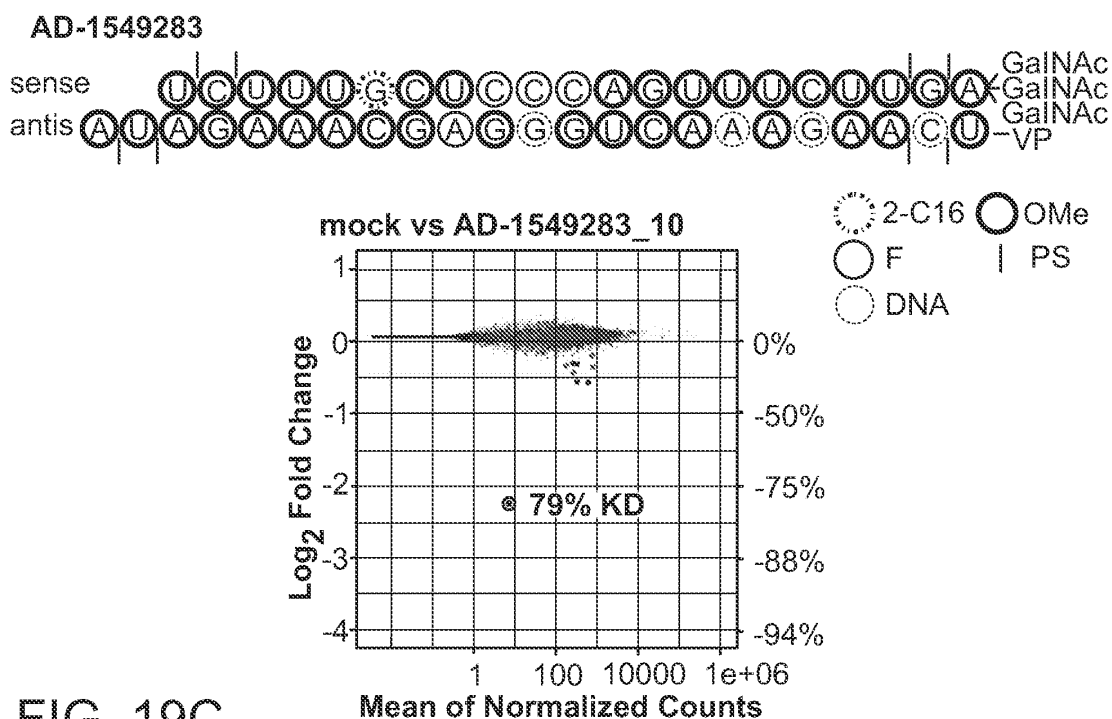
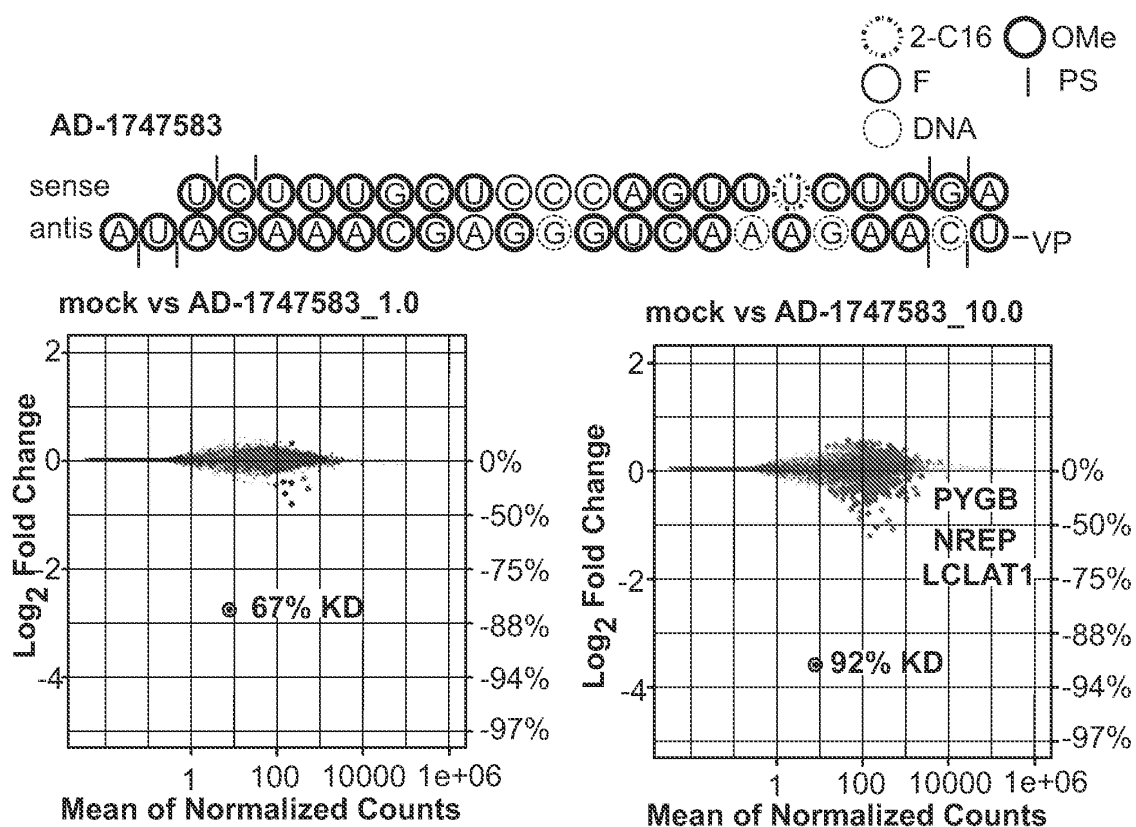
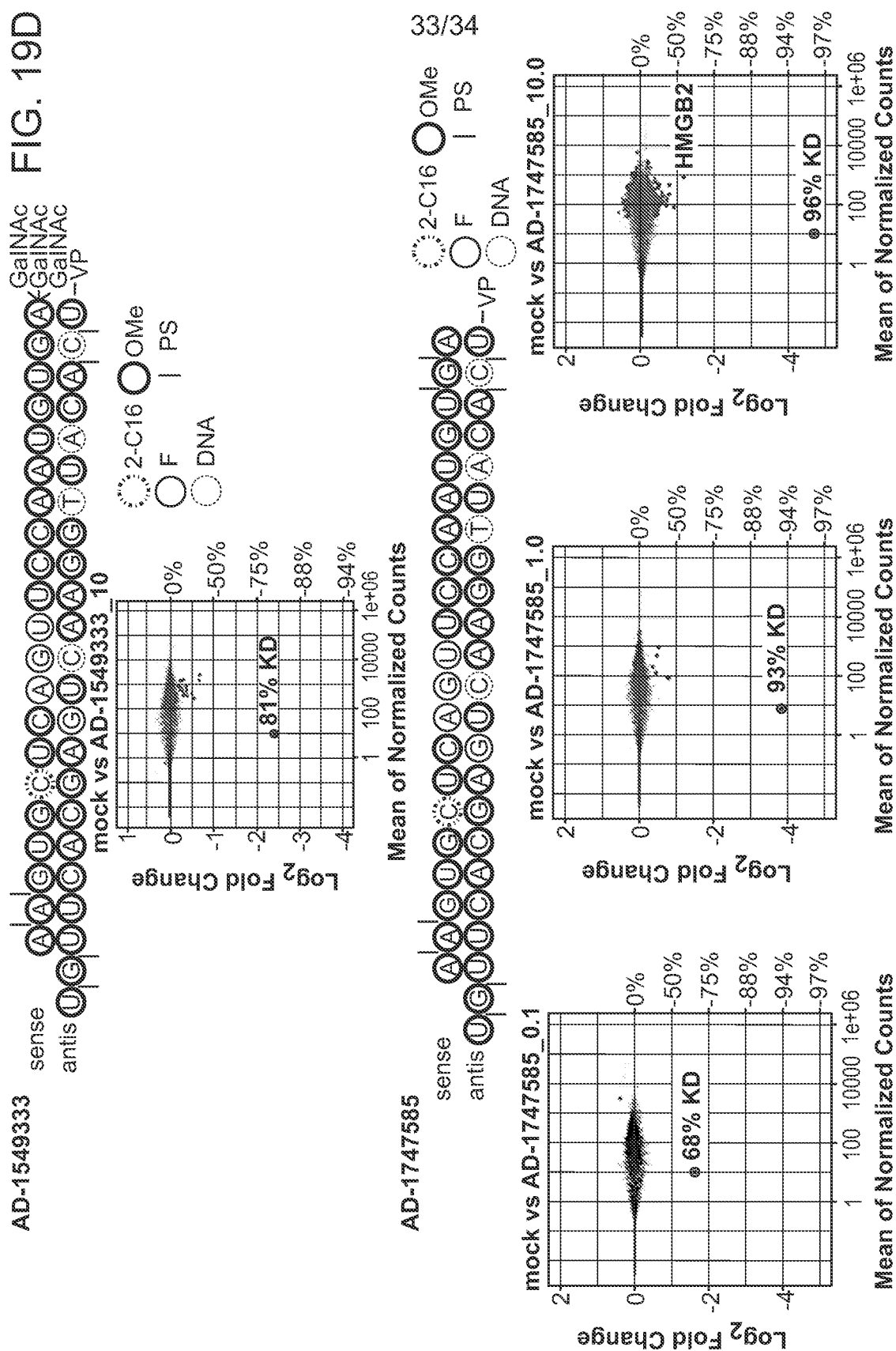


FIG. 19C





		Target sequence Location	mRNA		Protein			Protein (redosed)		RNAseq	
			Maximal % knockdown Cortex D84	Maximal % knockdown Midbrain D84	Maximal % KD CSF D83/D85	Mean % KD Cortex D84	Mean % KD Midbrain D84	Mean % KD** Cortex D85	Mean % KD** Midbrain D85		Dysregulated Genes >50%
AD-1747585		UTR	93.1	51.5	75.5	72.7	61.3	64.0	62.0		1
AD-1747583		UTR	96.6	83.7	91.2	98.5	66.0	70.0	57.3		3
AD-1747580		CDS	94.4	85.4	90.4	84.1	71.9	84.9	69.5		0

FIG. 20